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                  E GARBER D/AU
L73             5 SEA ABB=ON  PLU=ON  GARBER DAVID/AU
L74            40 SEA ABB=ON  PLU=ON  GARBER DAVID W?/AU
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L76            29 SEA ABB=ON  PLU=ON  DATTA G ?/AU
L77            44 SEA ABB=ON  PLU=ON  DATTA GEETA/AU
L78           134 SEA ABB=ON  PLU=ON  (L72 OR L73 OR L74 OR L75 OR L76 OR L77)
L79         23936 SEA ABB=ON  PLU=ON  APOLIPOPROTEIN?/OBI OR APO E/OBI OR
                  APOE/OBI
L80            31 SEA ABB=ON  PLU=ON  L79 AND L78
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L82             1 SEA ABB=ON  PLU=ON  L80 AND POLYPEPTIDE#/OBI
L83            20 SEA ABB=ON  PLU=ON  L81 OR L82
L84            19 SEA ABB=ON  PLU=ON  L83 NOT L71
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=> FIL REG
FILE 'REGISTRY' ENTERED AT 12:49:55 ON 22 MAY 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   19 MAY 2006  HIGHEST RN 885029-44-7
DICTIONARY FILE UPDATES:  19 MAY 2006  HIGHEST RN 885029-44-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

*********************************************************************
*                                                                   *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                   *
*********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

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FILE 'CAPLUS' ENTERED AT 12:50:02 ON 22 MAY 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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hydrophobic acis

claim 1

FILE COVERS 1907 - 22 May 2006 VOL 144 ISS 22
FILE LAST UPDATED: 19 May 2006 (20060519/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

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L74 40 SEA FILE=CAPLUS ABB=ON PLU=ON GARBER DAVID W?/AU
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L77 44 SEA FILE=CAPLUS ABB=ON PLU=ON DATTA GEETA/AU
L78 134 SEA FILE=CAPLUS ABB=ON PLU=ON (L72 OR L73 OR L74 OR L75 OR L76 OR L77)
L79 23936 SEA FILE=CAPLUS ABB=ON PLU=ON APOLIPOPROTEIN?/OBI OR APO E/OBI OR APOE/OBI
L80 31 SEA FILE=CAPLUS ABB=ON PLU=ON L79 AND L78
L81 20 SEA FILE=CAPLUS ABB=ON PLU=ON L80 AND (PEPTIDE#/OBI OR POLYPEPETIDE#/OBI)
L82 1 SEA FILE=CAPLUS ABB=ON PLU=ON L80 AND POLYPEPTIDE#/OBI
L83 20 SEA FILE=CAPLUS ABB=ON PLU=ON L81 OR L82
L84 19 SEA FILE=CAPLUS ABB=ON PLU=ON L83 NOT L71

L> inverter search.

=> D .CA HITSTR L71;D .CA L84 1-19

L71 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:430718 CAPLUS
DOCUMENT NUMBER: 141:1254
TITLE: Synthetic single domain polypeptides mimicking apolipoprotein E that enhance low and very low density lipoprotein uptake, reduce serum cholesterol and reduce risk of cardiovascular disease
INVENTOR(S): Anantharamiah, Gattadahalli M.; Garber, David W.; Datta, Geeta
PATENT ASSIGNEE(S): The UAB Research Foundation, USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004043403	A2	20040527	WO 2003-US36268	20031113

WO 2004043403 A3 20051215
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2514303 AA 20040527 CA 2003-2514303 20031113
AU 2003290825 A1 20040603 AU 2003-290825 20031113
US 2004186057 A1 20040923 US 2003-712447 20031113
EP 1599173 A2 20051130 EP 2003-783409 20031113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRIORITY APPLN. INFO.: US 2002-425821P P 20021113
WO 2003-US36268 W 20031113

OTHER SOURCE(S): MARPAT 141:1254
ED Entered STN: 27 May 2004
AB The present invention provides novel synthetic apolipoprotein E (ApoE)-mimicking peptides wherein the receptor binding domain of ApoE is covalently linked to 18L, the well characterized lipid-associating model class L amphipathic helical peptide. Such peptides enhance low d. lipoprotein (LDL) and very low d. lipoprotein (VLDL) binding to and degradation by fibroblast or HepG2 cells. Also provided are possible applications of the synthetic peptides in lowering human plasma LDL cholesterol levels, thus inhibiting atherosclerosis or cardiovascular diseases.
IC ICM A61K
CC 1-8 (Pharmacology)
Section cross-reference(s): 3, 6, 14
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(amino acid sequence; synthetic polypeptides mimicking ApoE that enhance LDL and VLDL uptake, reduce serum cholesterol and reduce risk of cardiovascular disease)

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RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; synthetic polypeptides mimicking ApoE that enhance LDL and VLDL uptake, reduce serum cholesterol and reduce risk of cardiovascular disease)

RN 697226-63-4 CAPLUS
CN Glycine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-leucylglycyl-L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-isoleucyl-L-arginyl-L-alanyl-L-phenylalanyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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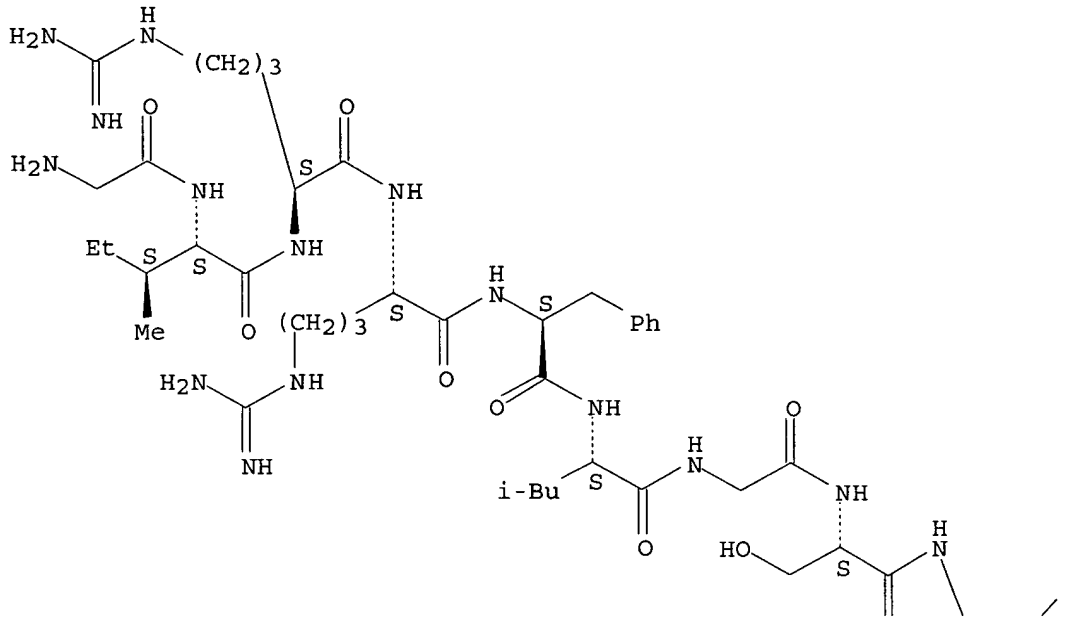

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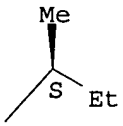

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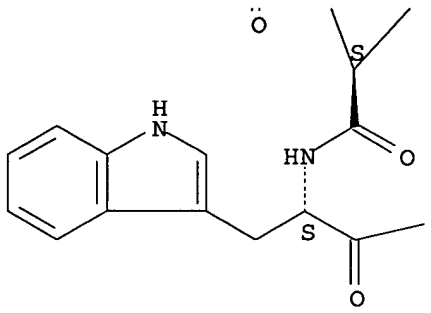

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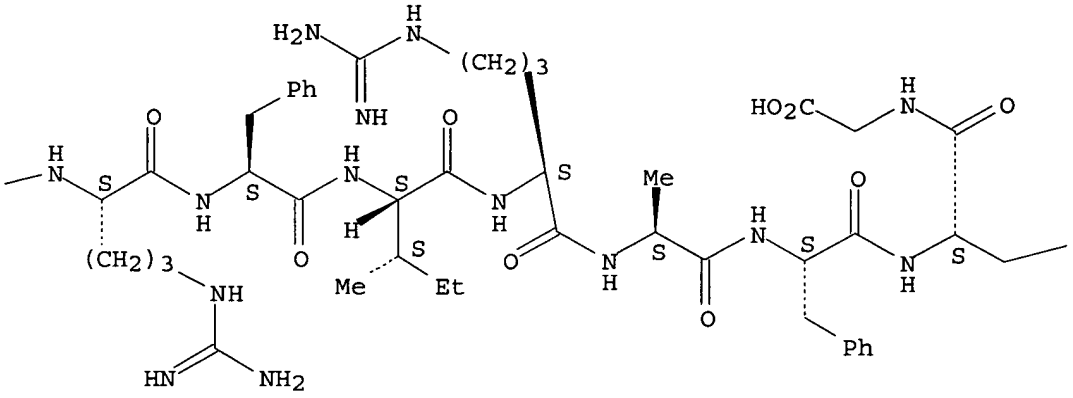

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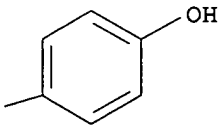

RN 697226-64-5 CAPLUS
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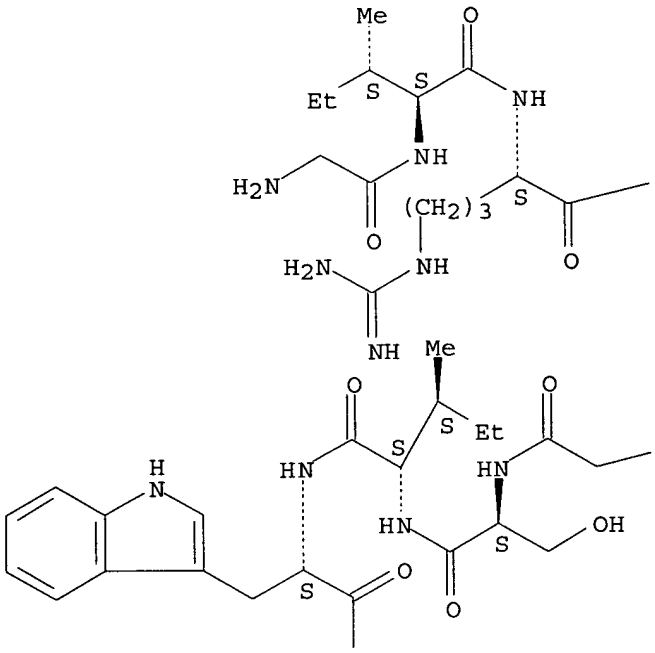
Absolute stereochemistry.

PAGE 1-A



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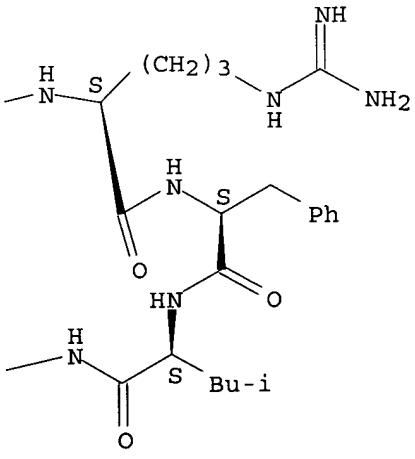

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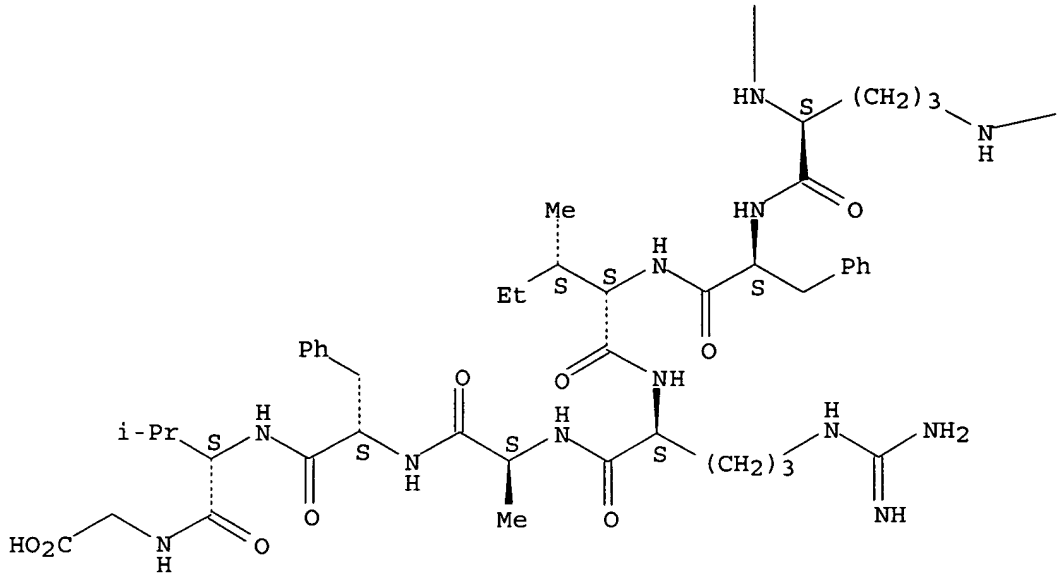

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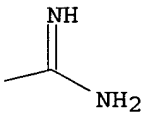

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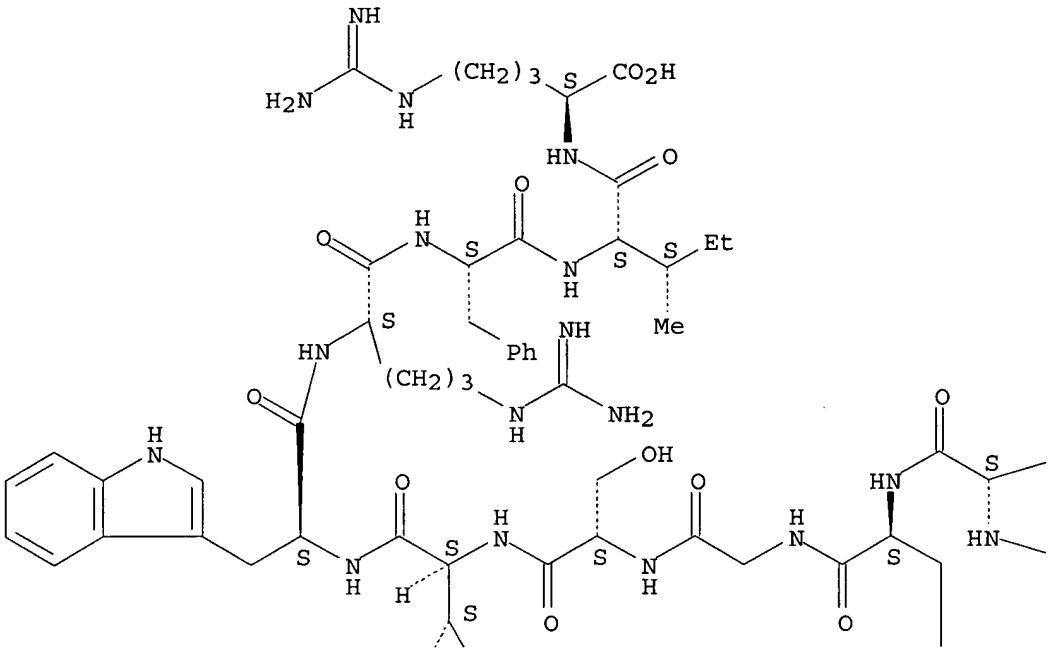
Absolute stereochemistry.

PAGE 1-A



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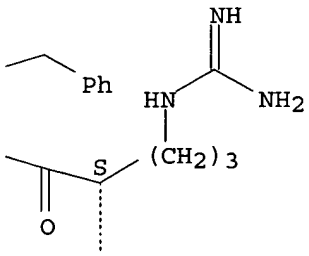

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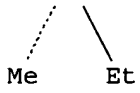

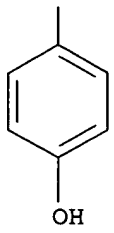

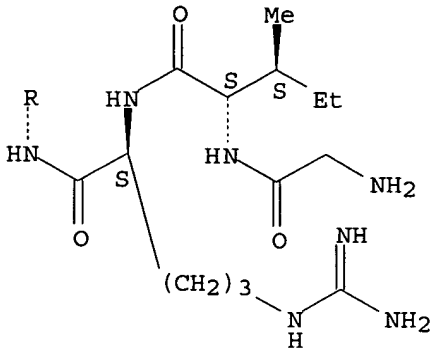

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RN 697226-72-5 CAPLUS
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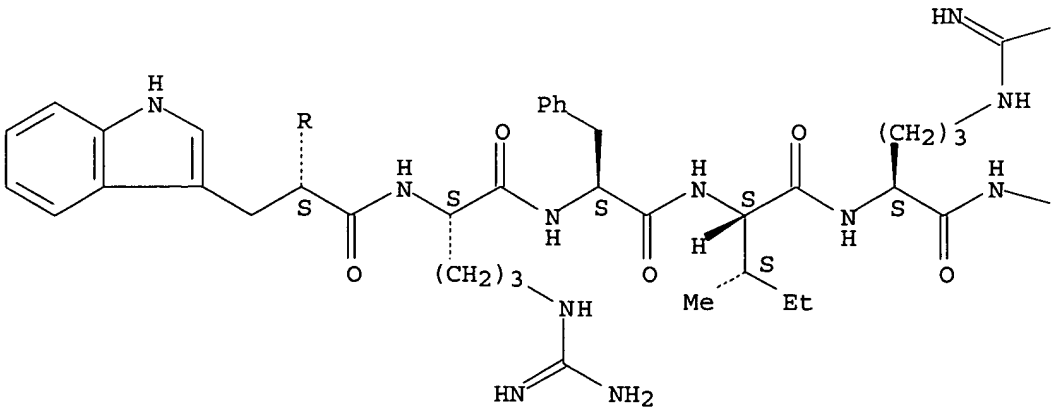
Absolute stereochemistry.

PAGE 1-A



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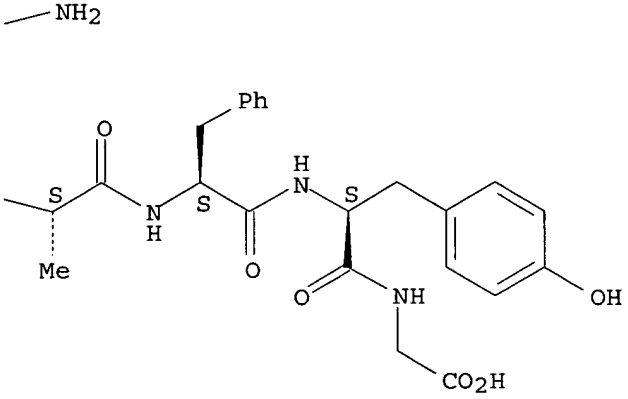

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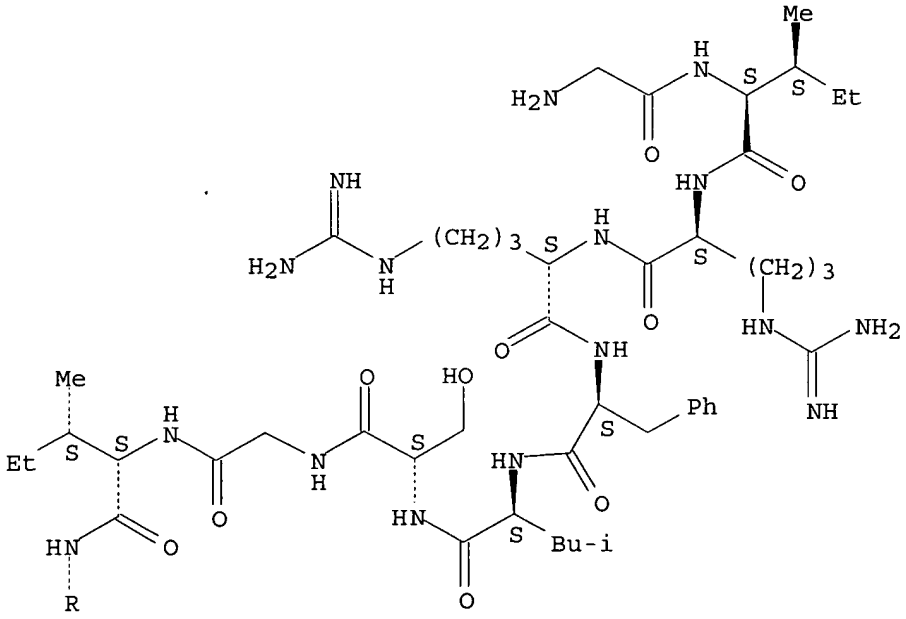

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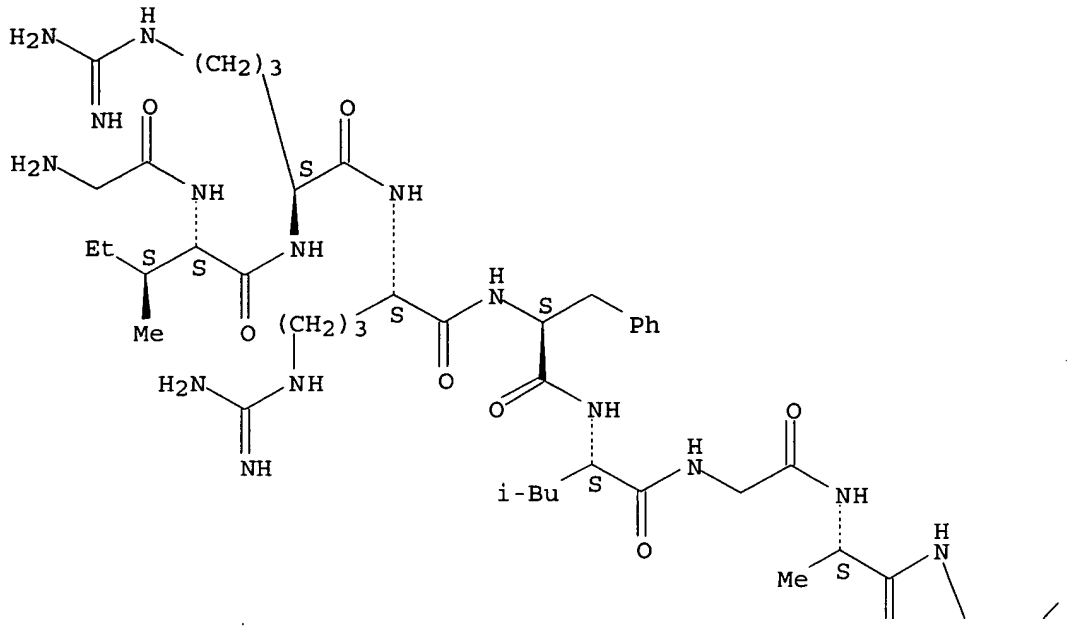
Absolute stereochemistry.

PAGE 1-A



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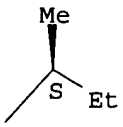

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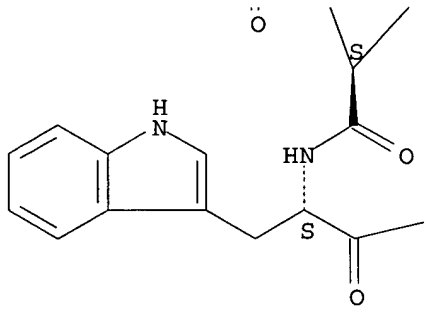

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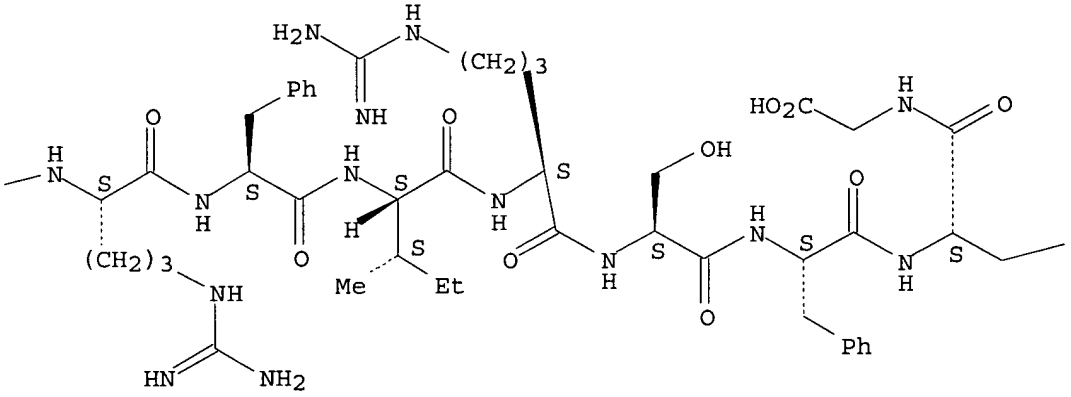

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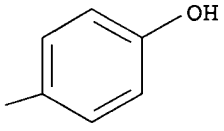
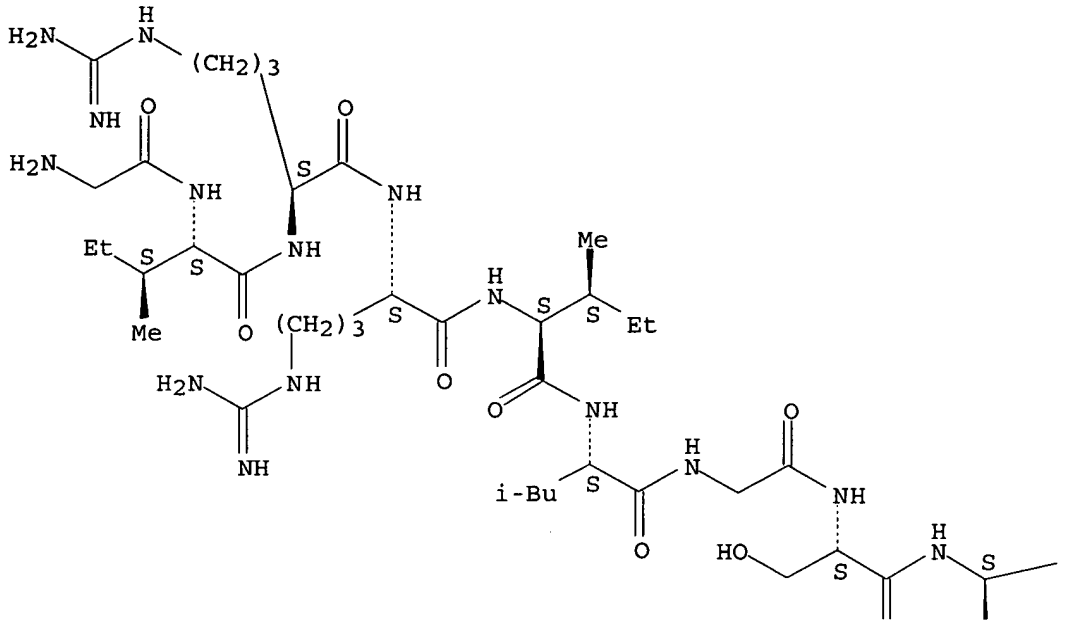


RN 697227-58-0 CAPLUS
CN Glycine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-isoleucyl-L-leucylglycyl-L-seryl-L-phenylalanyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-phenylalanyl-L-arginyl-L-alanyl-L-isoleucyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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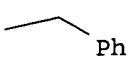

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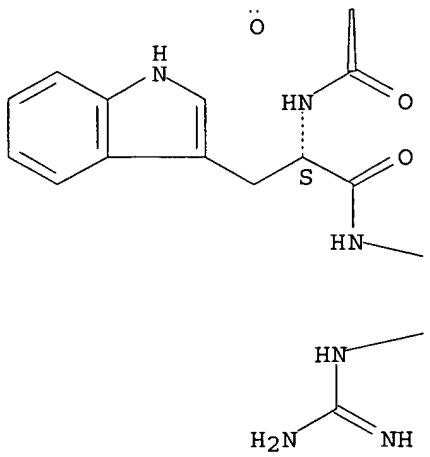

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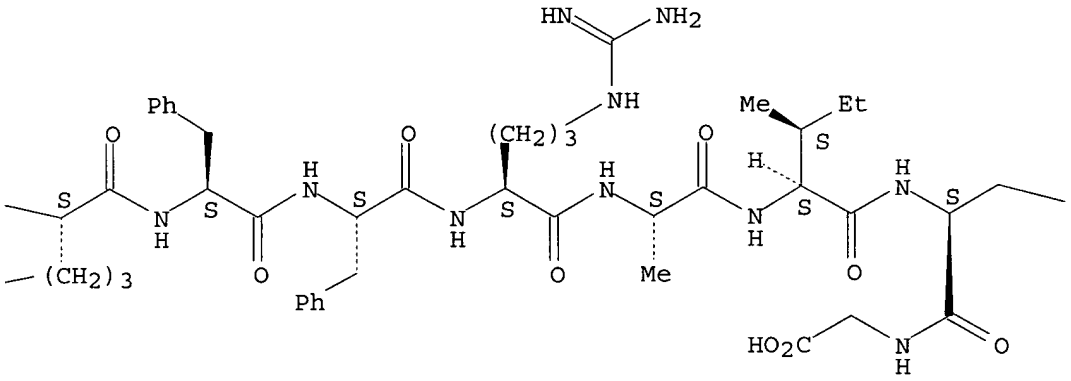

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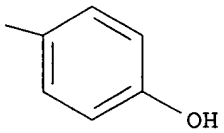
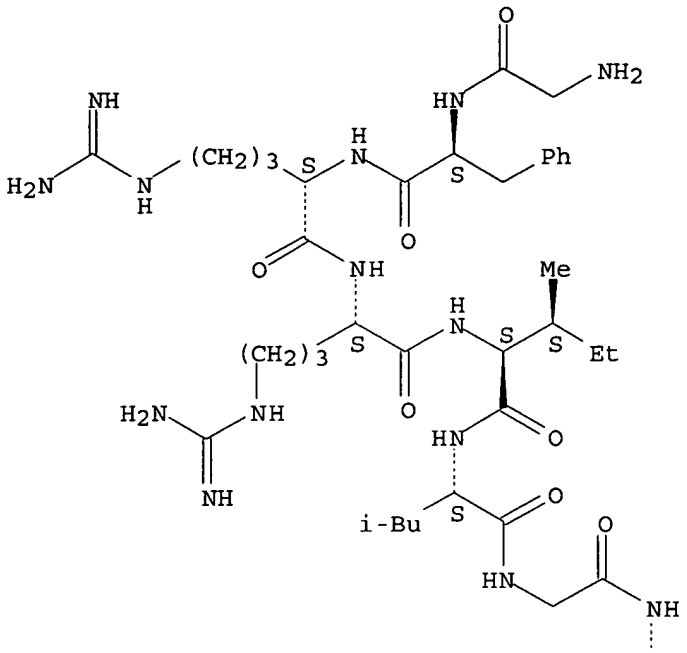


RN 697227-59-1 CAPLUS
CN Glycine, glycyl-L-phenylalanyl-L-arginyl-L-arginyl-L-isoleucyl-L-

leucylglycyl-L-seryl-L-phenylalanyl-L-tryptophyl-L-arginyl-L-isoleucyl-L-phenylalanyl-L-arginyl-L-alanyl-L-isoleucyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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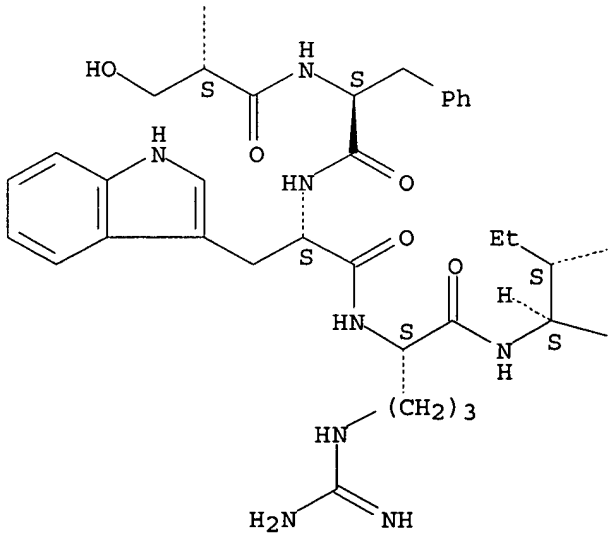

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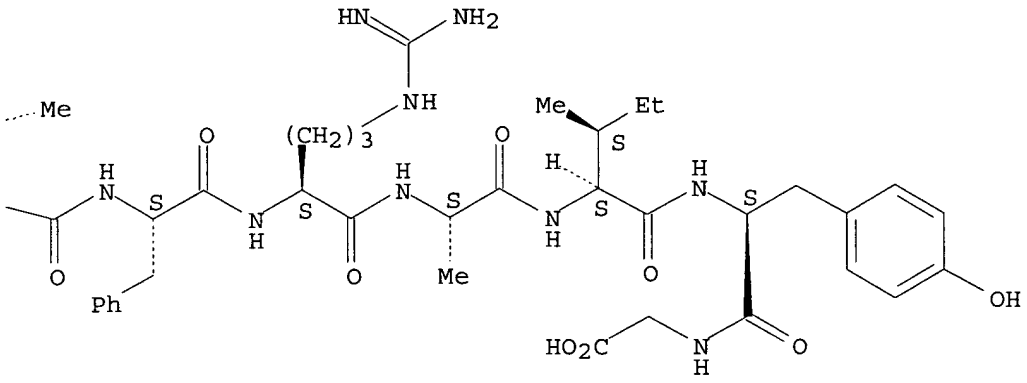
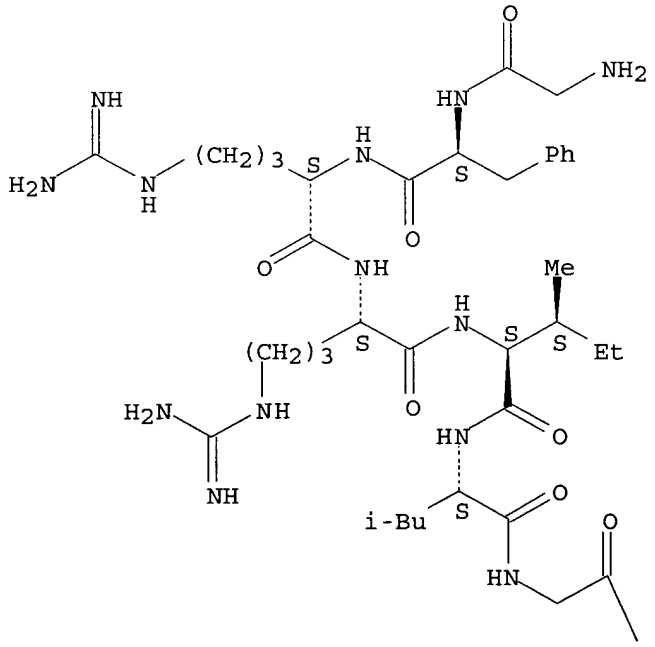


RN 697227-60-4 CAPLUS
CN Glycine, glycyl-L-phenylalanyl-L-arginyl-L-arginyl-L-isoleucyl-L-leucylglycyl-L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-isoleucyl-L-arginyl-L-alanyl-L-phenylalanyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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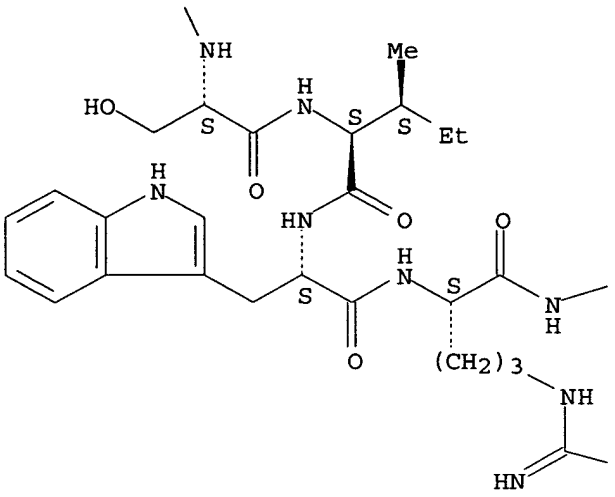

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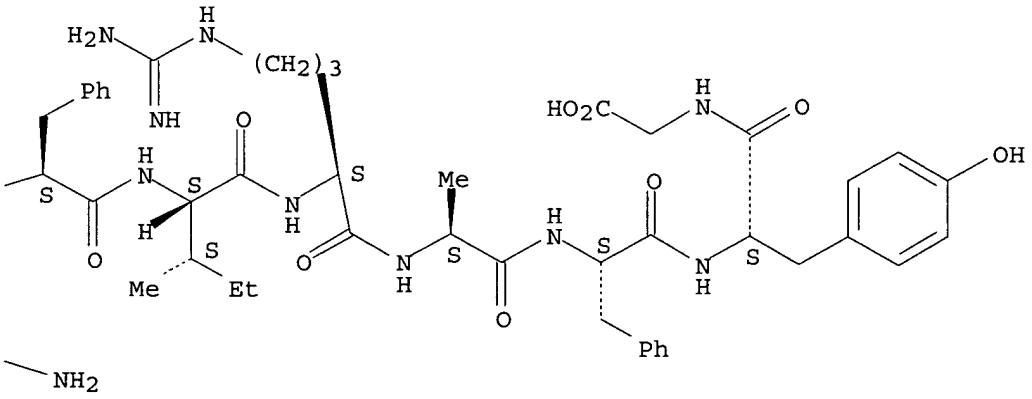

RN 697227-61-5 CAPLUS
CN Glycine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-leucylglycyl-L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-isoleucyl-L-phenylalanyl-L-arginyl-L-alanyl-L-phenylalanyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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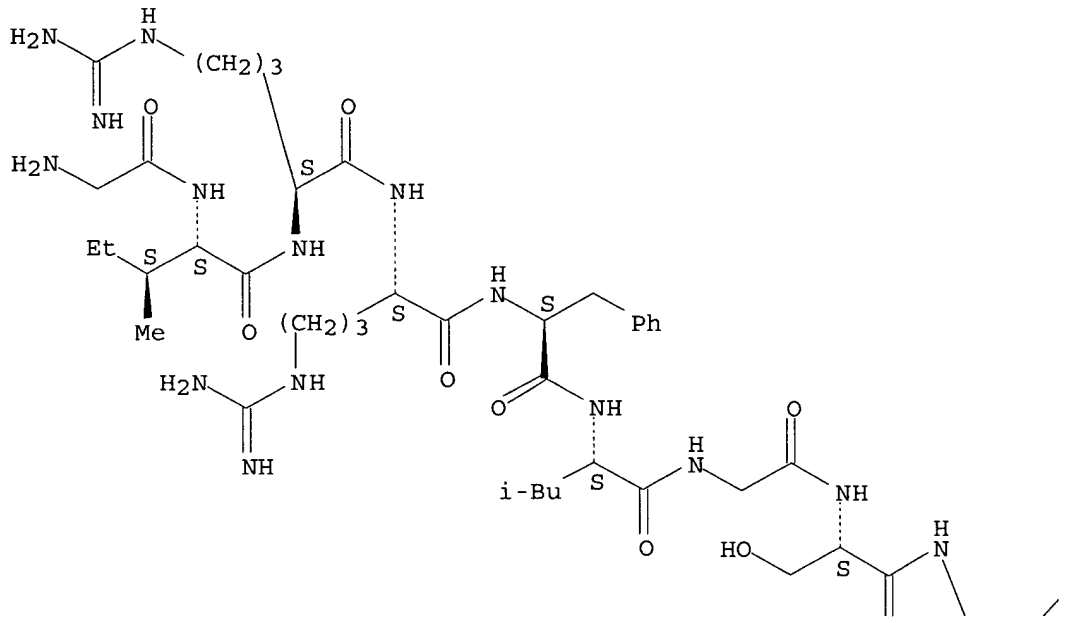

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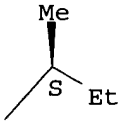

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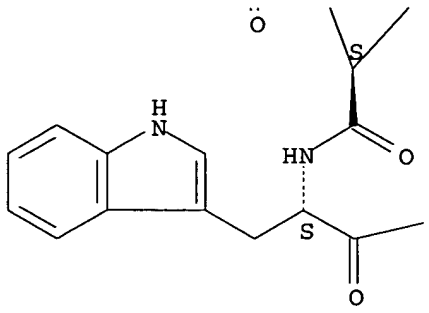

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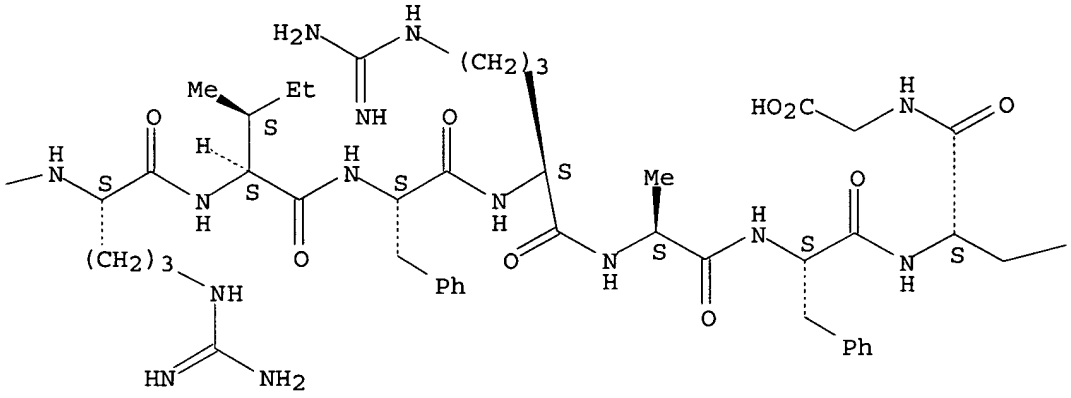

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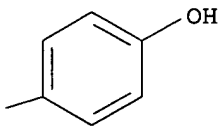

RN 697227-62-6 CAPLUS
CN Glycine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-leucylglycyl-L-seryl-L-phenylalanyl-L-tryptophyl-L-arginyl-L-isoleucyl-L-isoleucyl-L-arginyl-L-alanyl-L-phenylalanyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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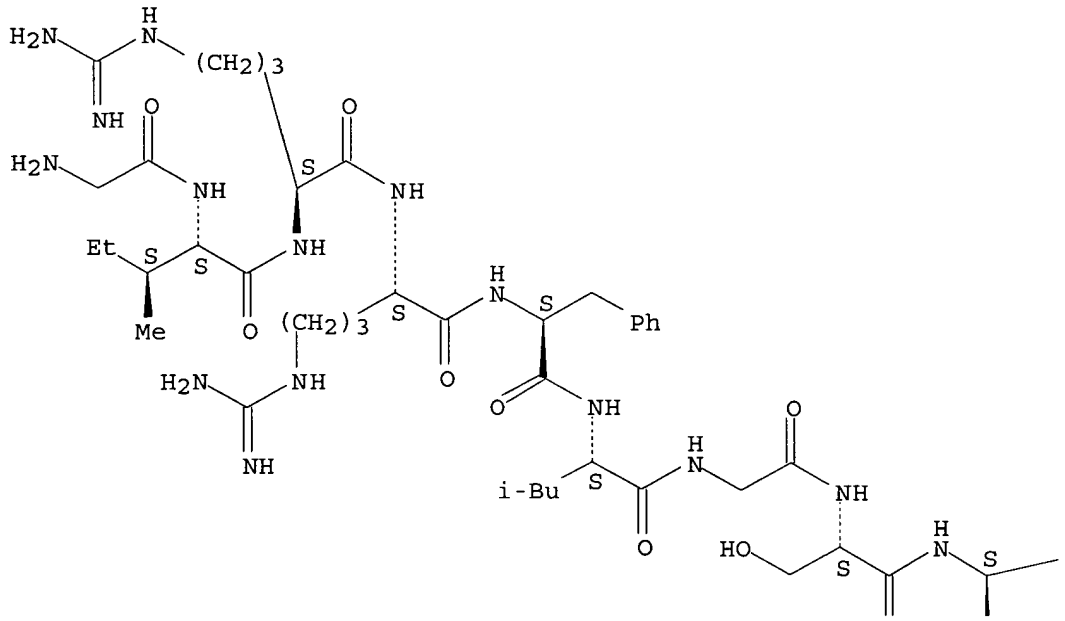

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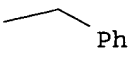

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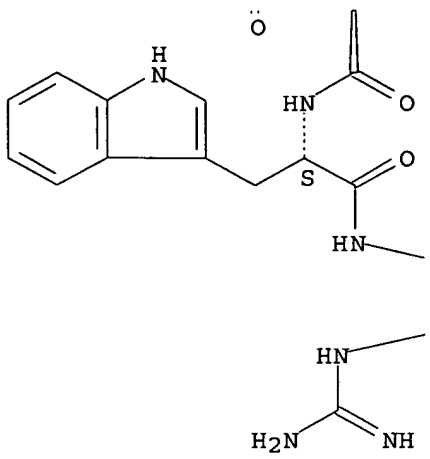

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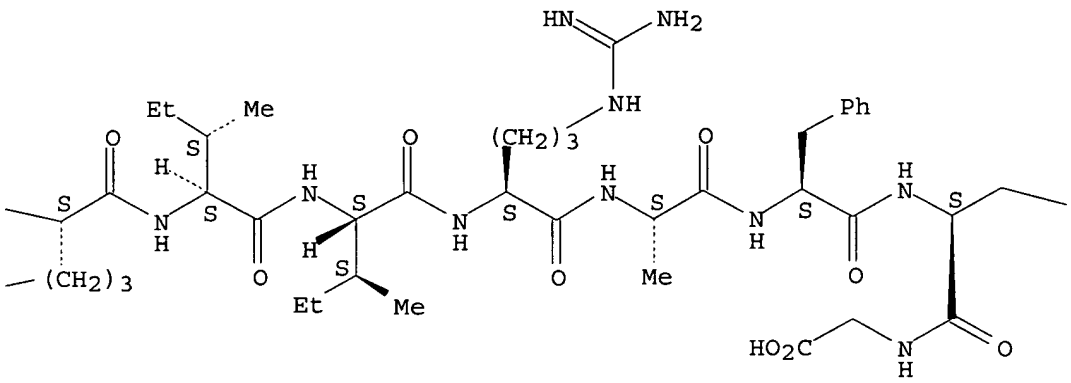

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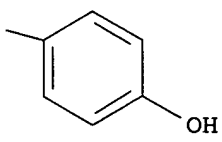

RN 697227-63-7 CAPLUS
CN Glycine, glycyl-L-leucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-

isoleucylglycyl-L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-isoleucyl-L-arginyl-L-alanyl-L-phenylalanyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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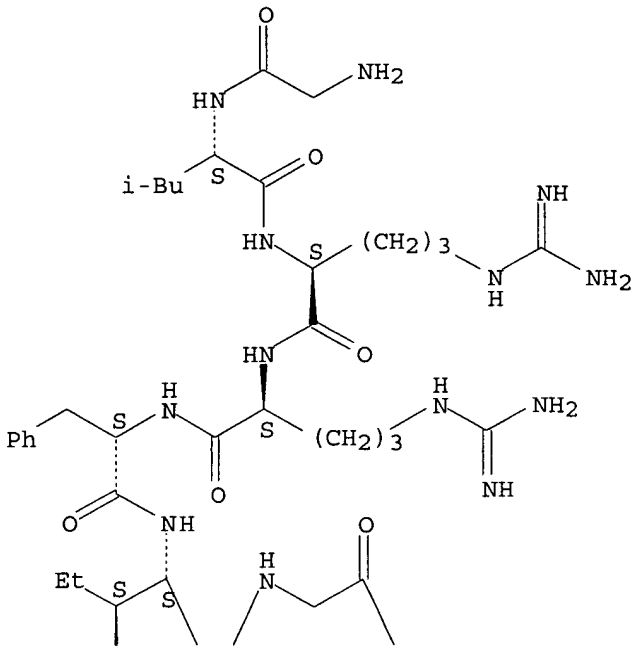

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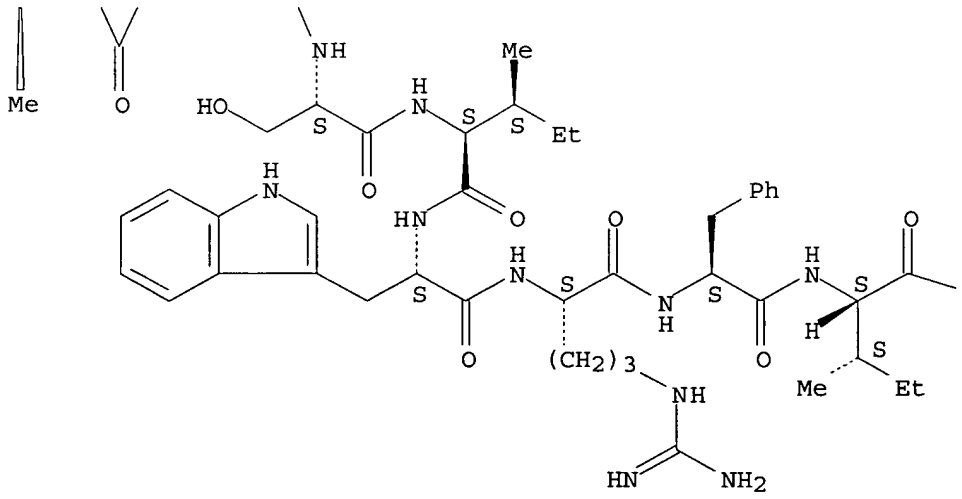

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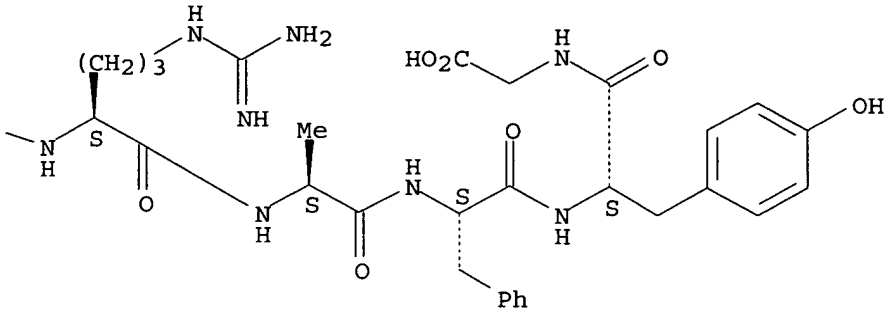

RN 697227-64-8 CAPLUS
CN Glycine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-isoleucylglycyl-L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-leucyl-L-arginyl-L-alanyl-L-phenylalanyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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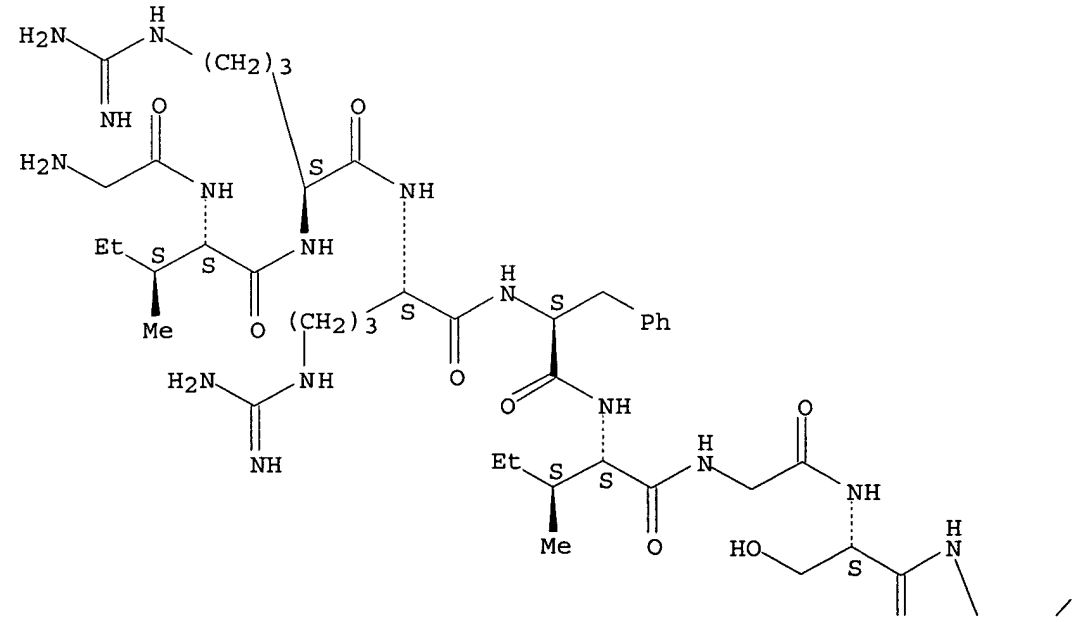

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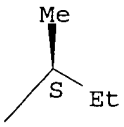

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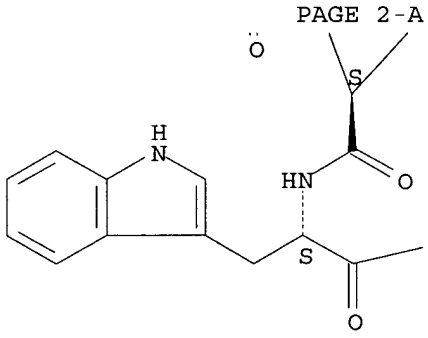

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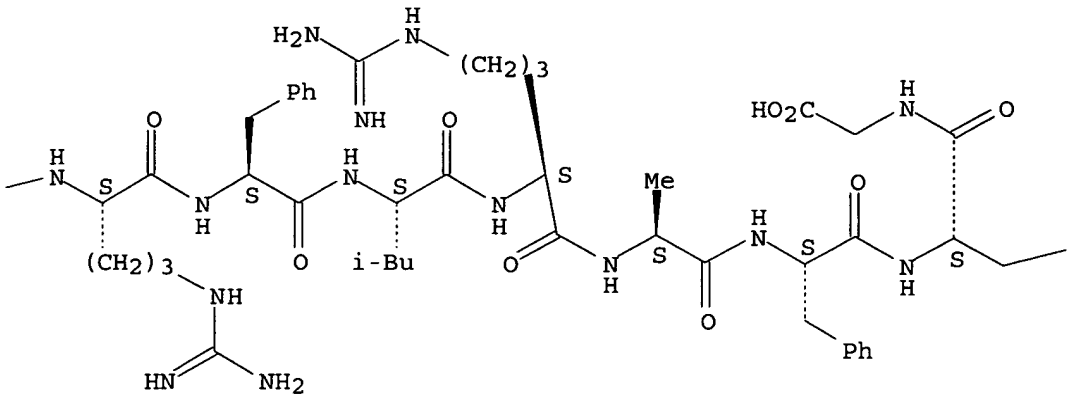

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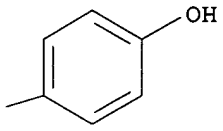

RN 697227-65-9 CAPLUS
CN Glycine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-leucylglycyl-L-seryl-L-phenylalanyl-L-tryptophyl-L-arginyl-L-isoleucyl-L-phenylalanyl-L-arginyl-L-alanyl-L-isoleucyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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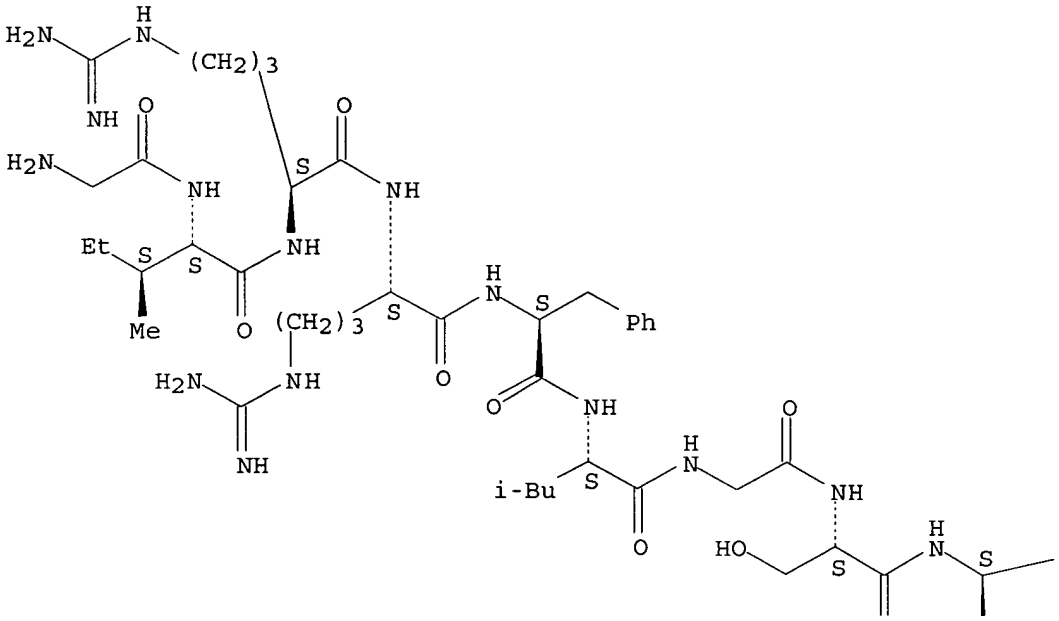

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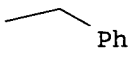

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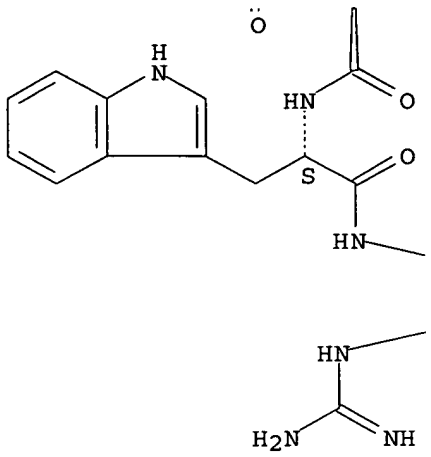

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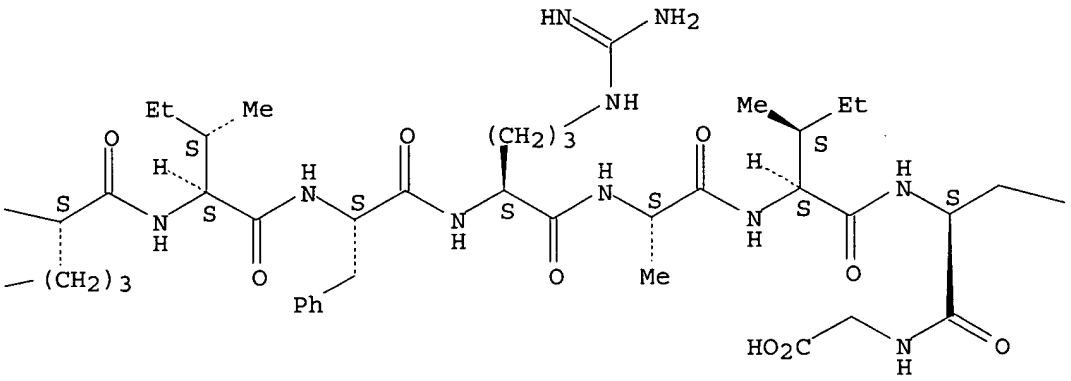

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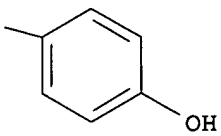

RN 697227-66-0 CAPLUS
CN Glycine, glycyl-L-phenylalanyl-L-arginyl-L-arginyl-L-phenylalanyl-L-

leucylglycyl-L-seryl-L-phenylalanyl-L-tryptophyl-L-arginyl-L-isoleucyl-L-isoleucyl-L-arginyl-L-alanyl-L-isoleucyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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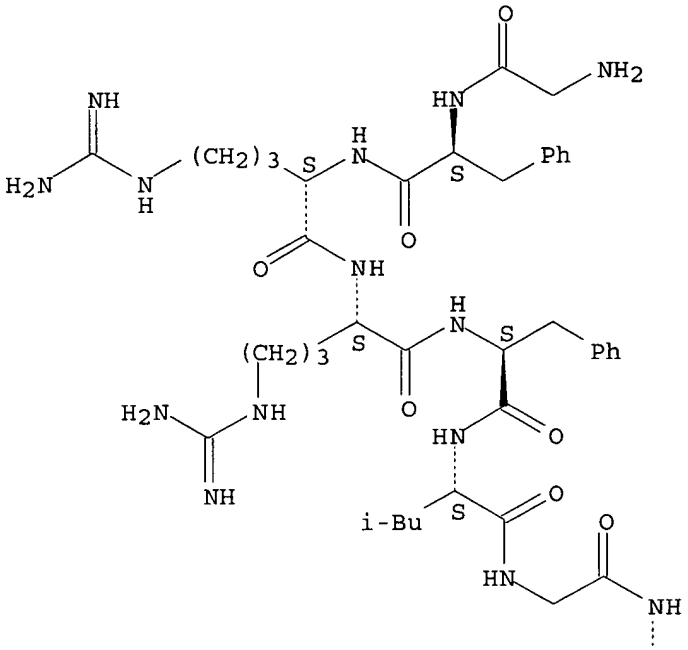

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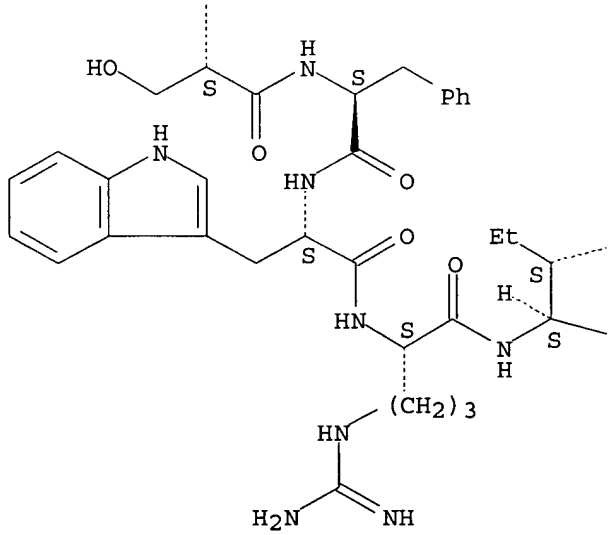

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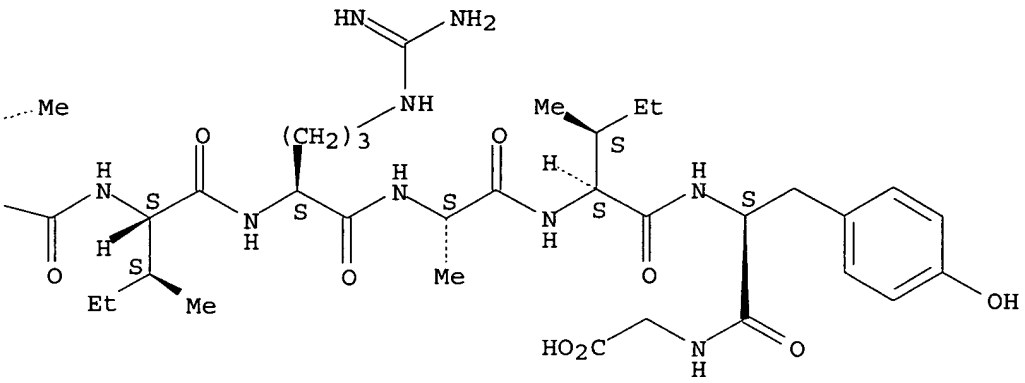

RN 697227-67-1 CAPLUS
CN Glycine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-leucylglycyl-L-seryl-L-isoleucyl-L-tyrosyl-L-arginyl-L-phenylalanyl-L-isoleucyl-L-arginyl-L-alanyl-L-phenylalanyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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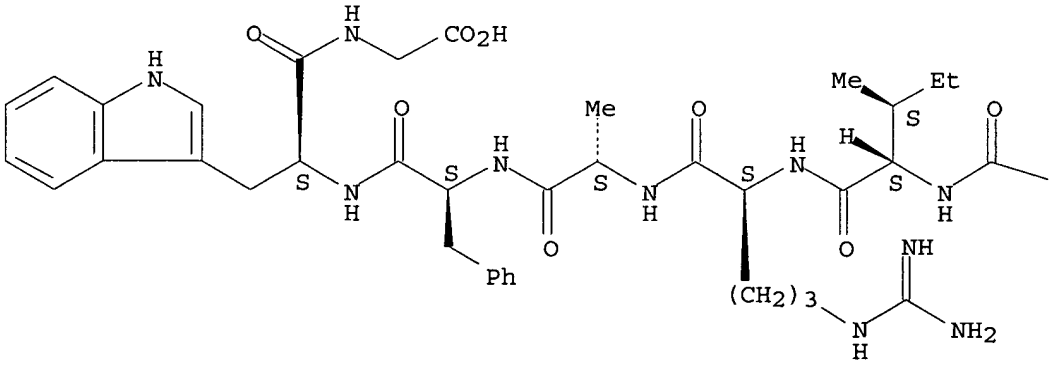

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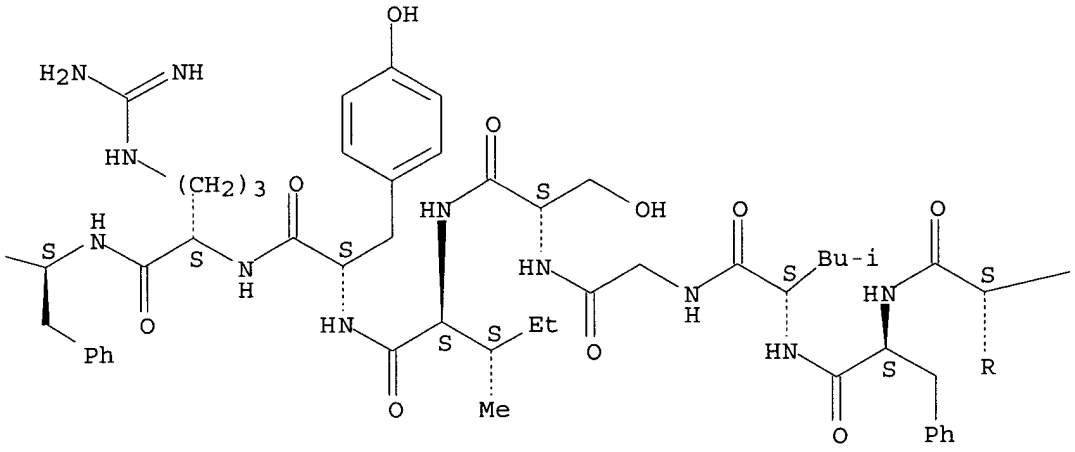

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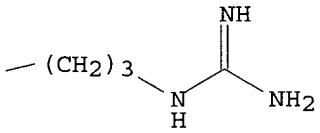

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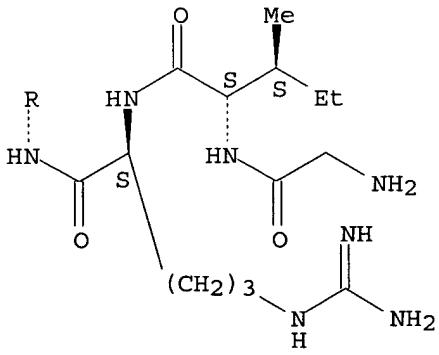

RN 697227-69-3 CAPLUS
CN Glycine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-tyrosylglycyl-L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-isoleucyl-L-arginyl-L-alanyl-L-phenylalanyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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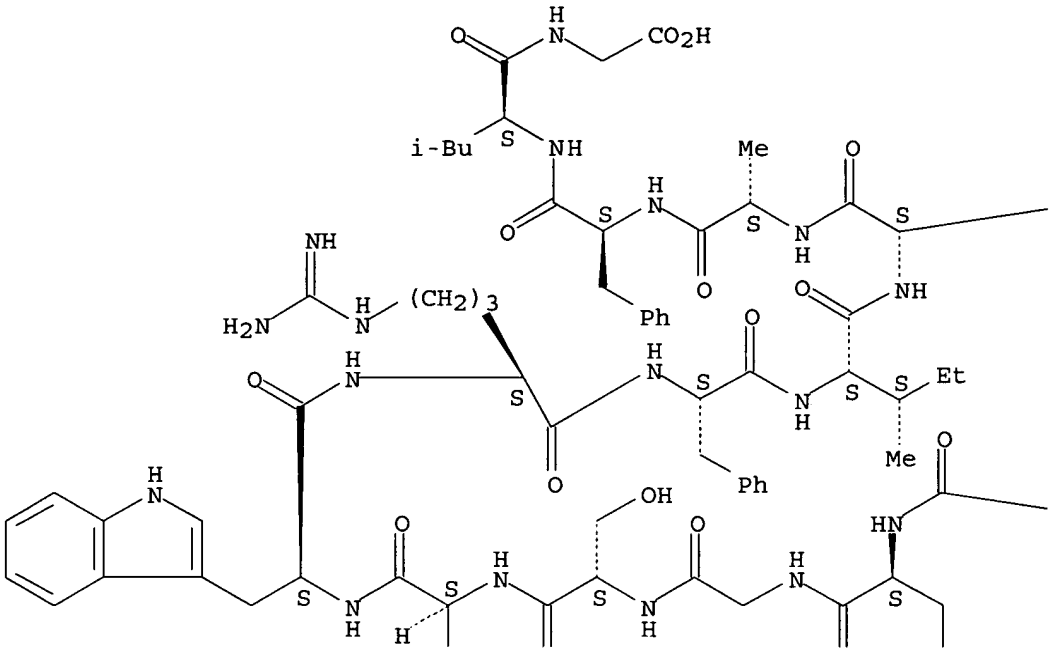

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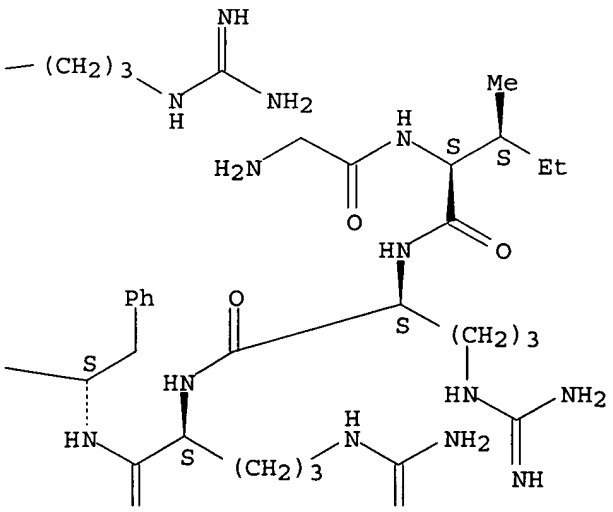

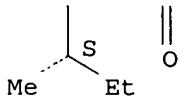

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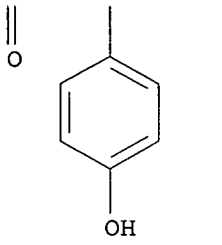

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RN 697227-76-2 CAPLUS
CN Glycine, glycyl-L-leucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-isoleucylglycyl-L-seryl-L-leucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-leucyl-L-arginyl-L-alanyl-L-phenylalanyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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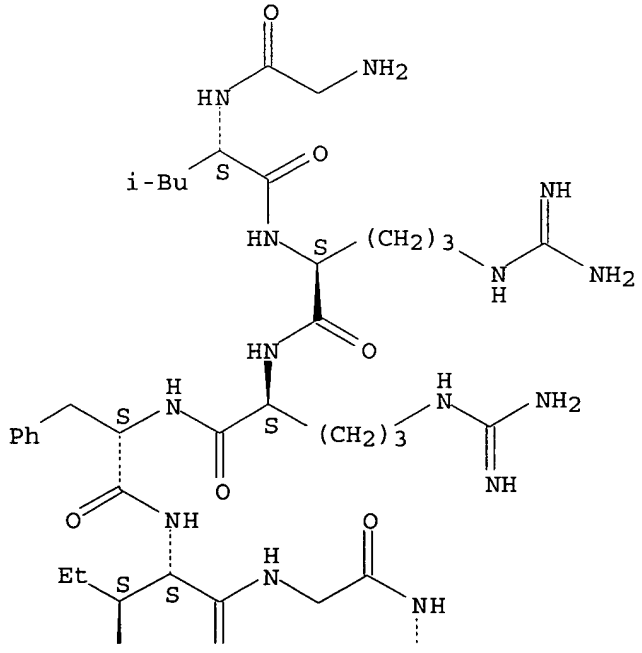

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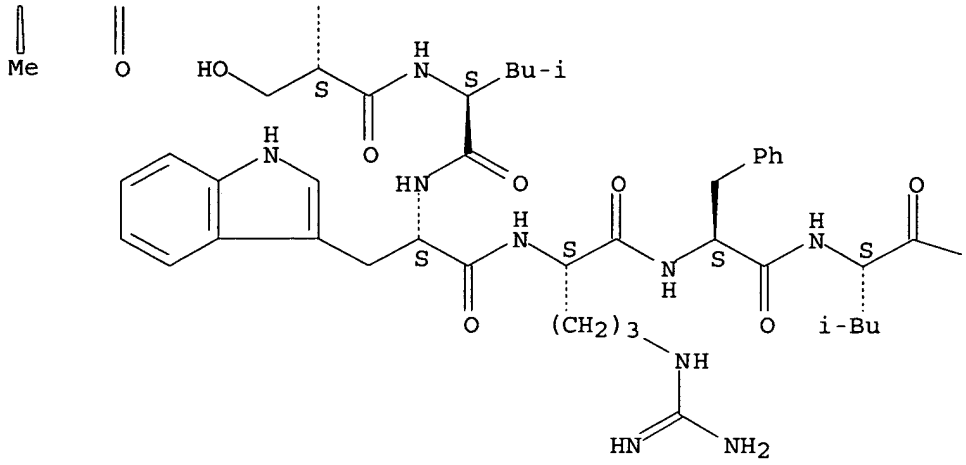

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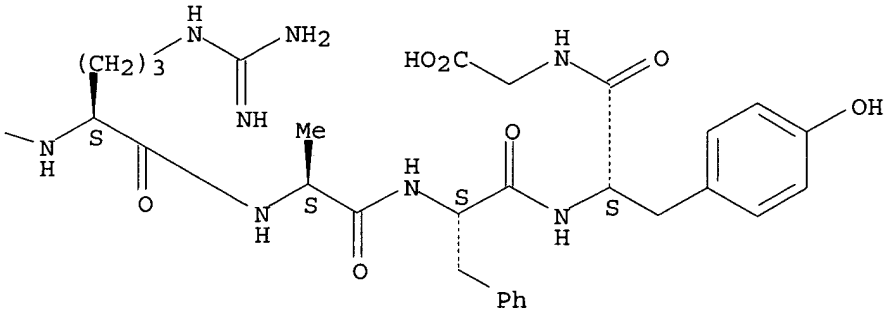
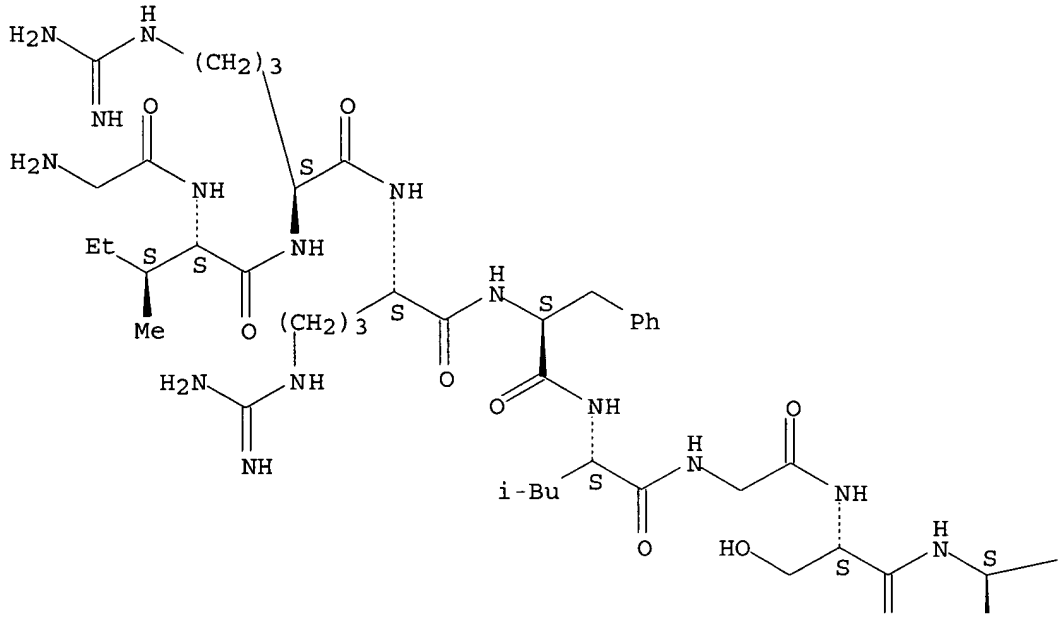


RN 697227-78-4 CAPLUS
CN Glycine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-leucylglycyl-L-seryl-L-leucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-leucyl-L-arginyl-L-alanyl-L-phenylalanyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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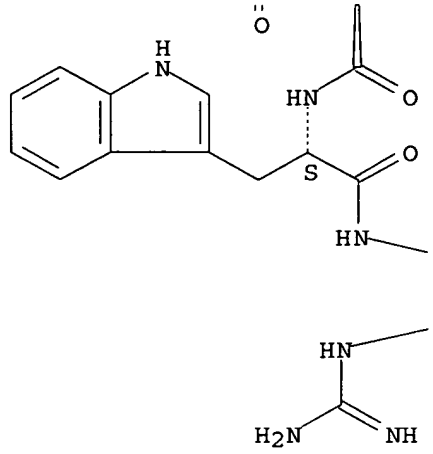
PAGE 2-A



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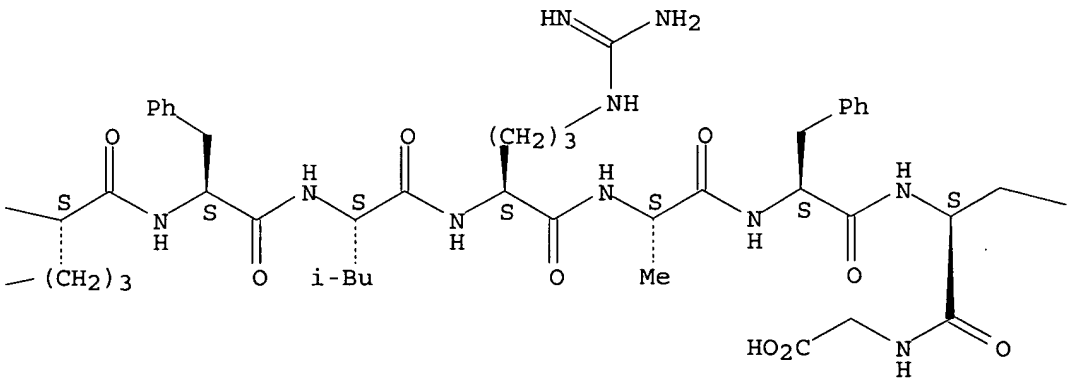

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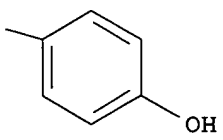
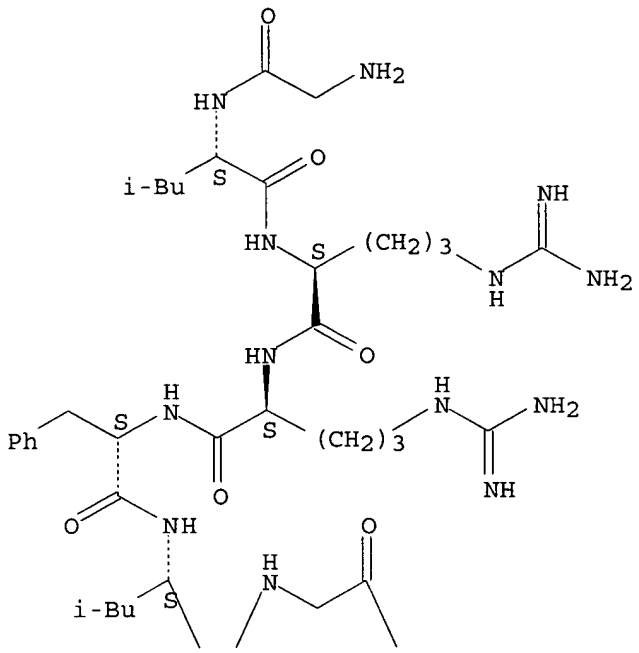


RN 697227-80-8 CAPLUS
CN Glycine, glycyl-L-leucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-leucylglycyl-

L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-leucyl-L-arginyl-L-alanyl-L-phenylalanyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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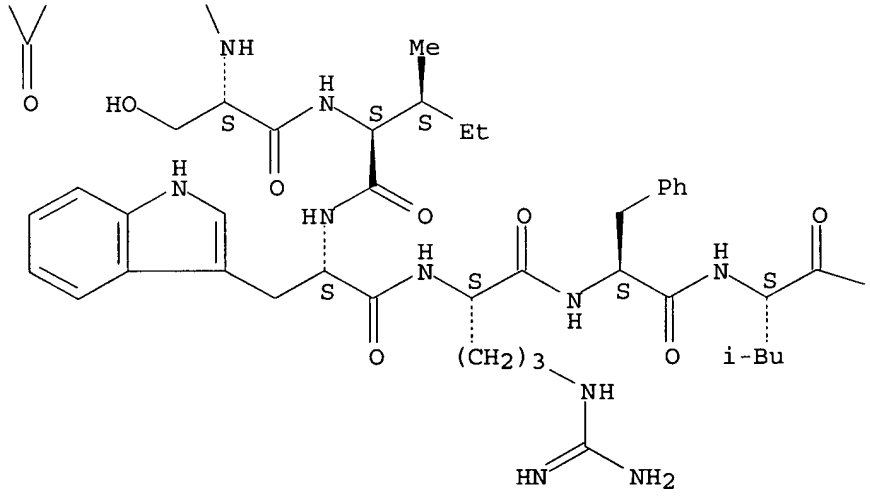

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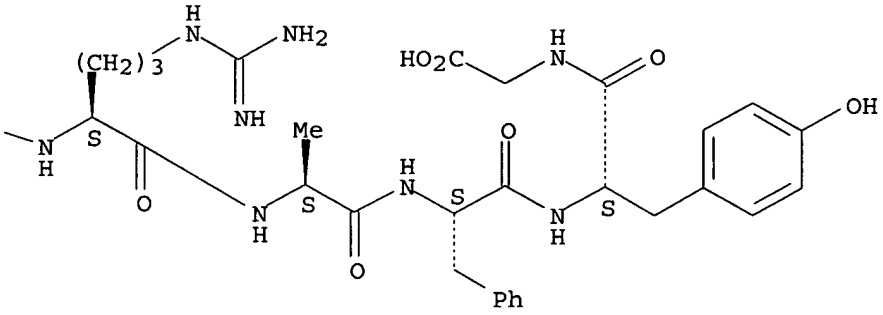
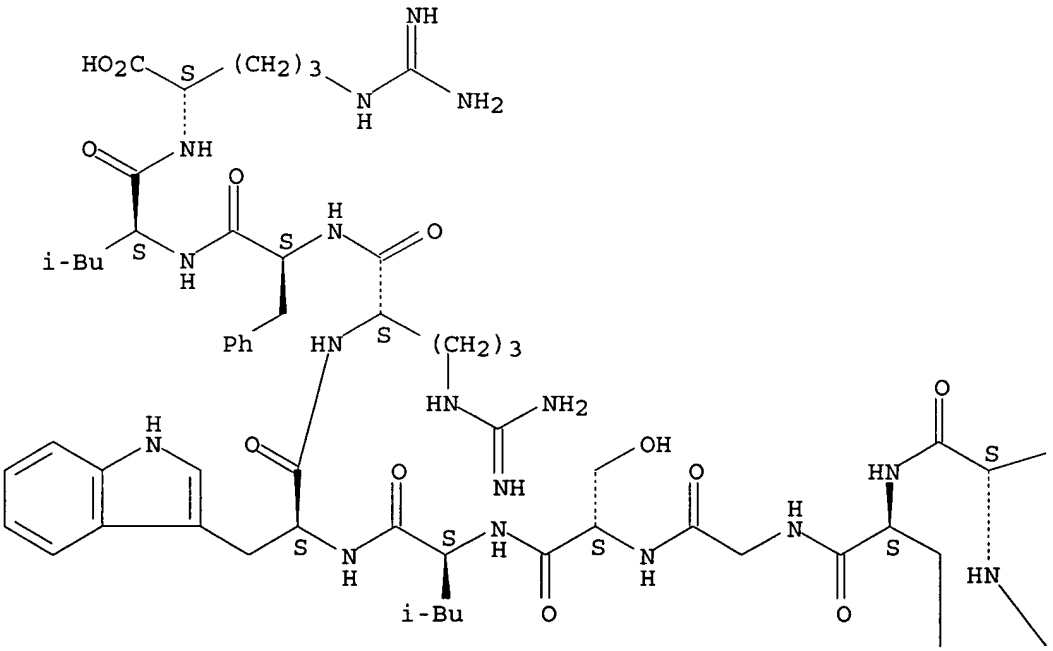


RN 697227-84-2 CAPLUS
CN L-Arginine, glycyl-L-leucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-tyrosylglycyl-L-seryl-L-leucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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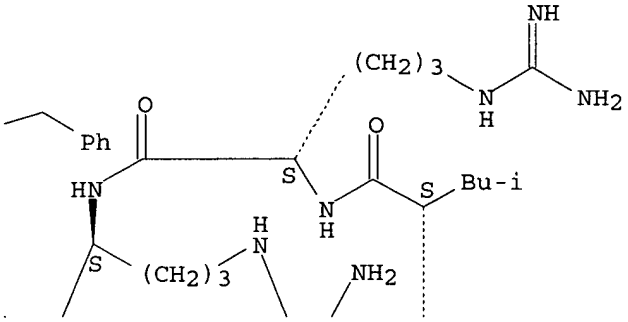

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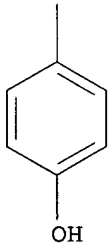

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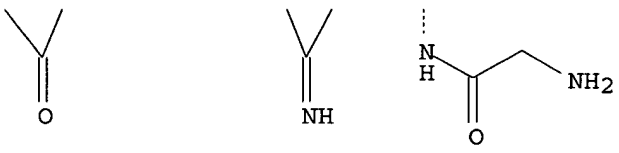
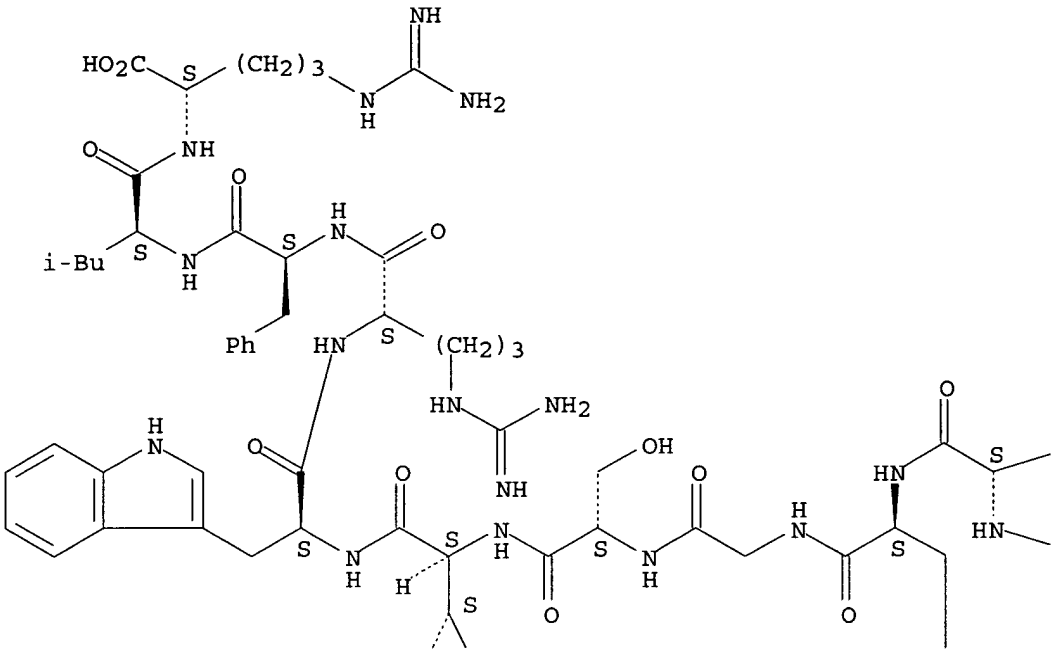


RN 697227-88-6 CAPLUS
CN L-Arginine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-tyrosylglycyl-L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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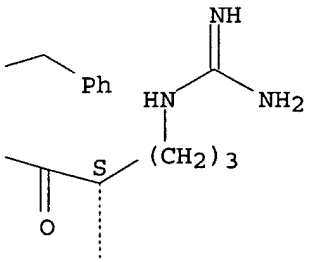

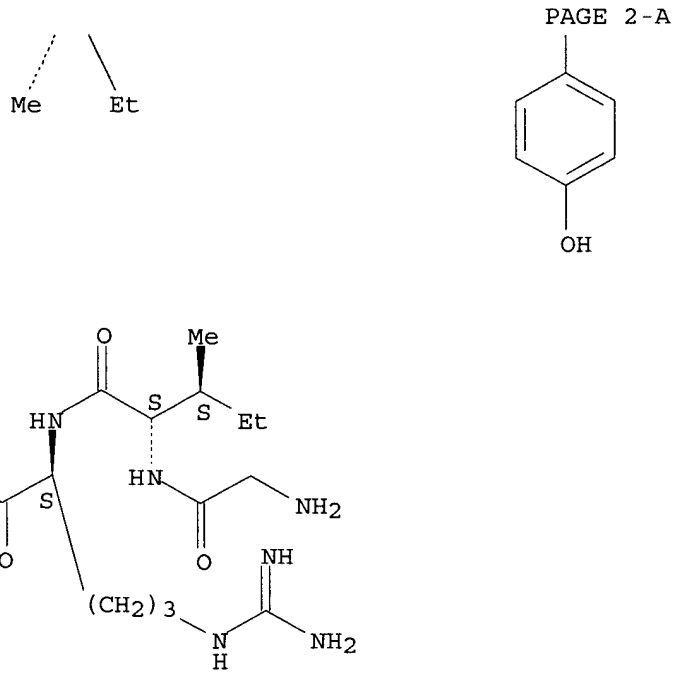

RN 697227-92-2 CAPLUS
CN L-Arginine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-tyrosylglycyl-L-seryl-L-leucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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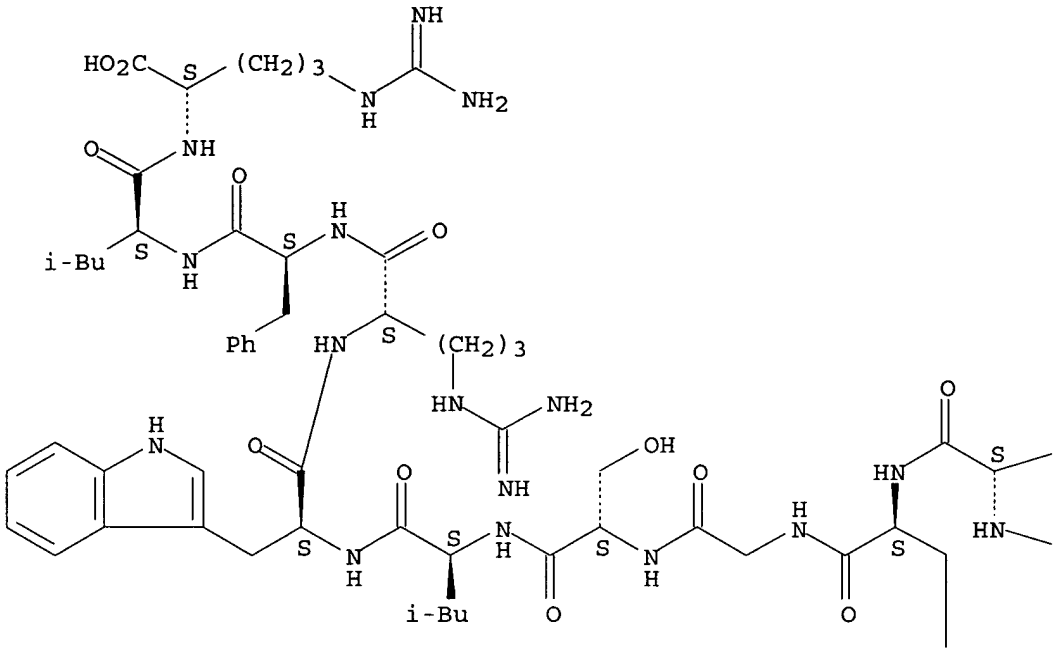

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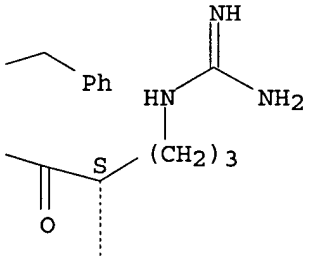

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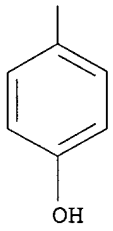

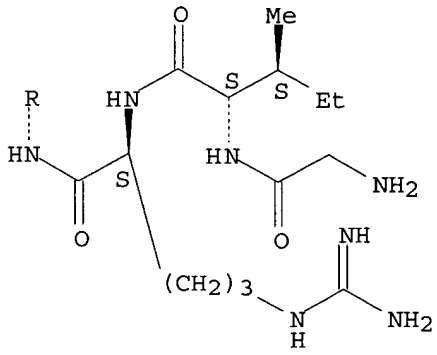

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RN 697227-95-5 CAPLUS
CN L-Arginine, glycyl-L-phenylalanyl-L-arginyl-L-arginyl-L-isoleucyl-L-tyrosylglycyl-L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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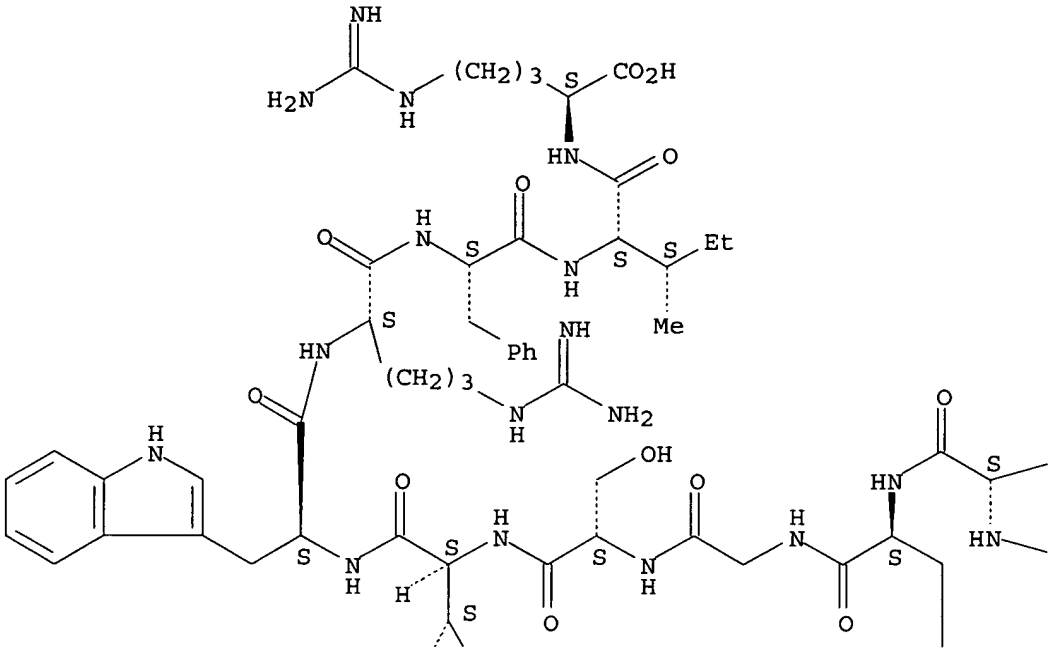

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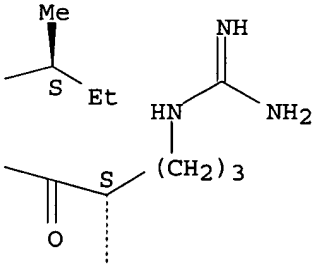

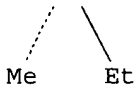

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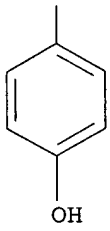

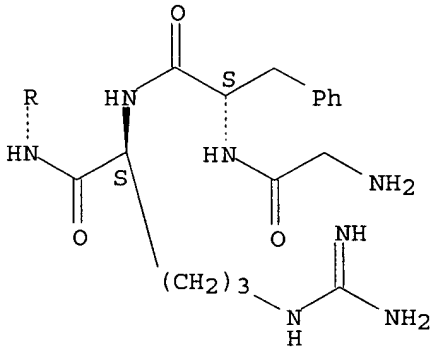

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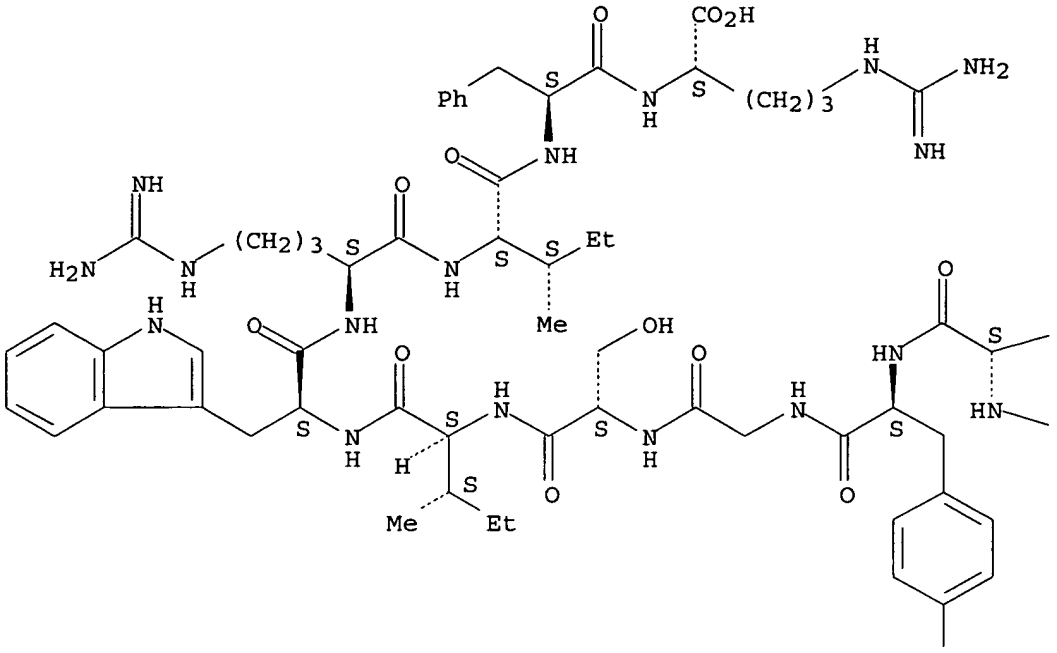
RN 697227-96-6 CAPLUS
CN L-Arginine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-tyrosylglycyl-L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-isoleucyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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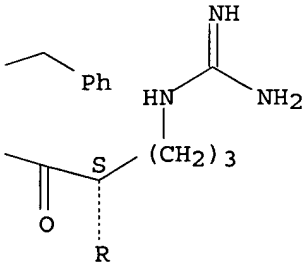

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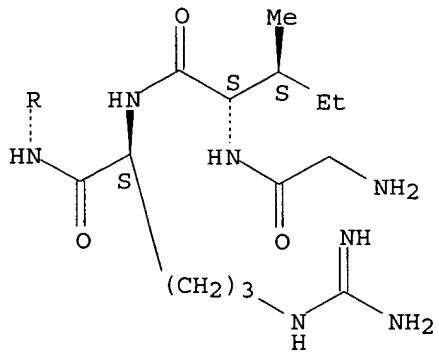

RN 697228-00-5 CAPLUS
CN L-Arginine, glycyl-L-leucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-tyrosylglycyl-L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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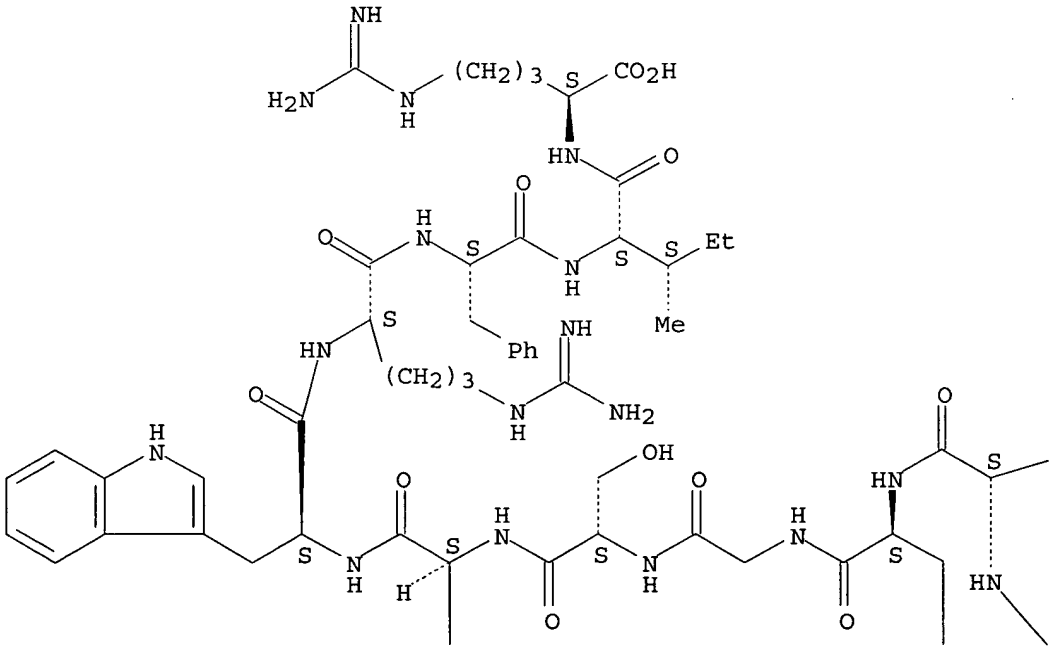

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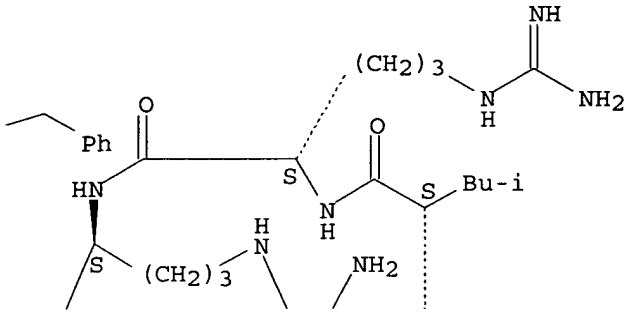

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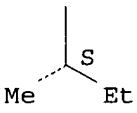

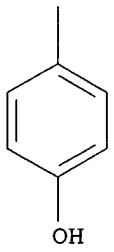

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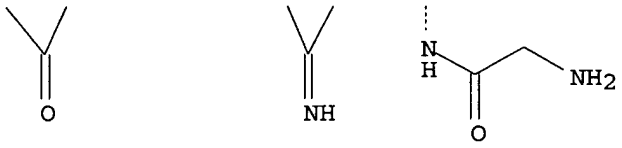
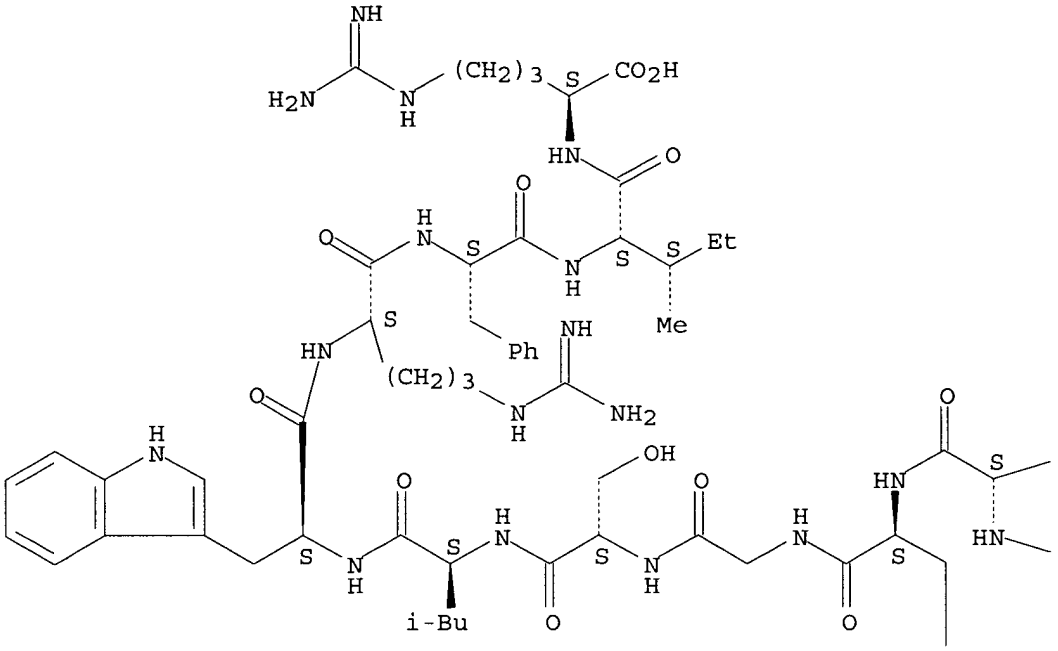


RN 697228-01-6 CAPLUS
CN L-Arginine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-phenylalanyl-L-tyrosylglycyl-L-seryl-L-leucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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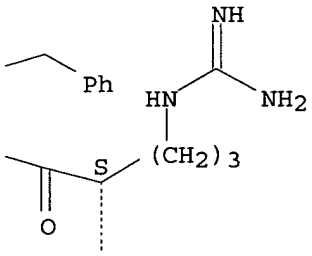

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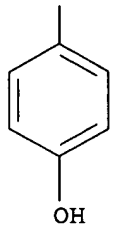

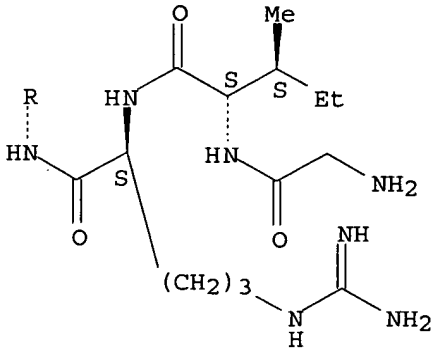

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RN 697228-02-7 CAPLUS
CN L-Arginine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-tyrosyl-L-phenylalanylglycyl-L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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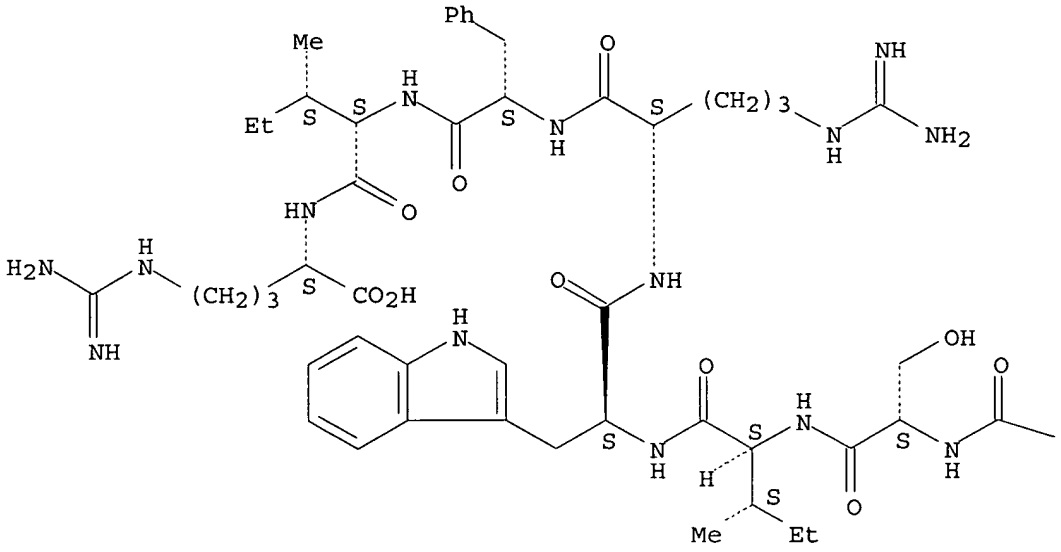

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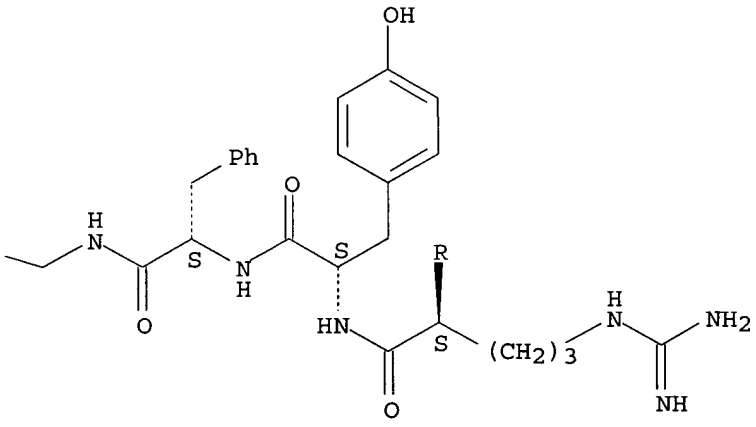

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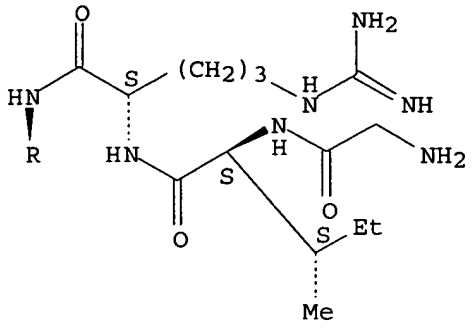

RN 697228-03-8 CAPLUS
CN L-Arginine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-tyrosyl-L-phenylalanylglycyl-L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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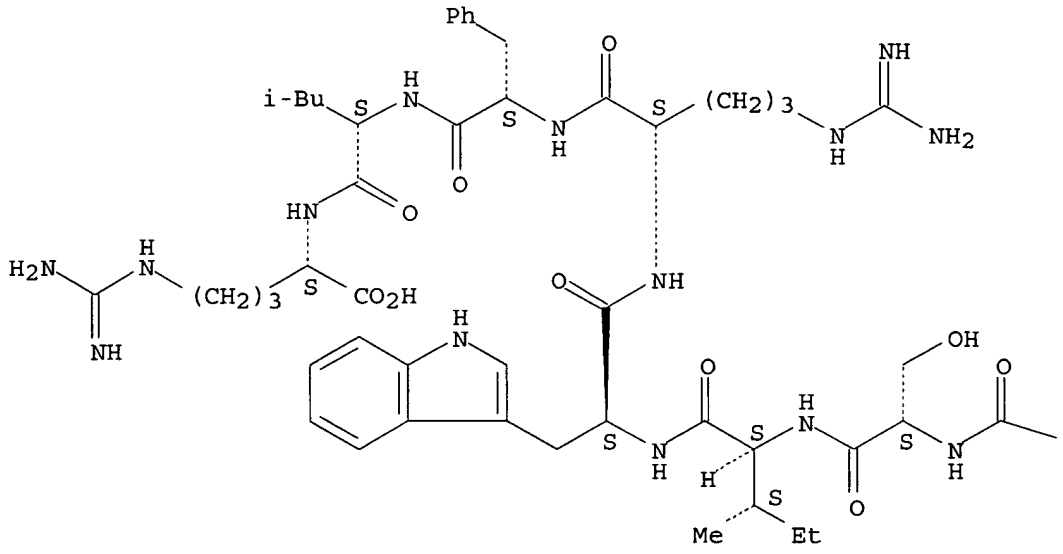

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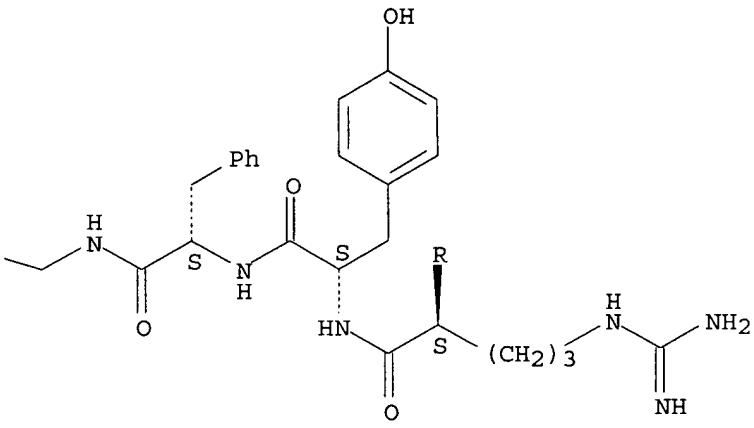

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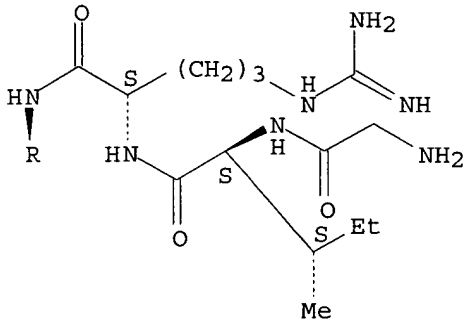

RN 697228-04-9 CAPLUS
CN L-Arginine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-tyrosyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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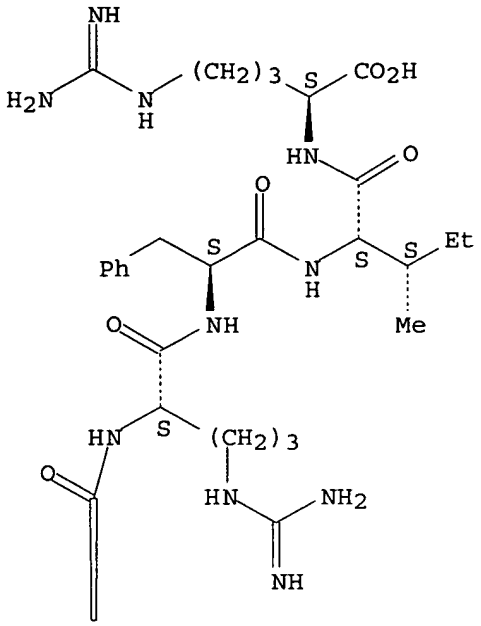

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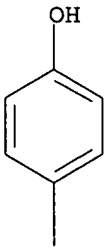

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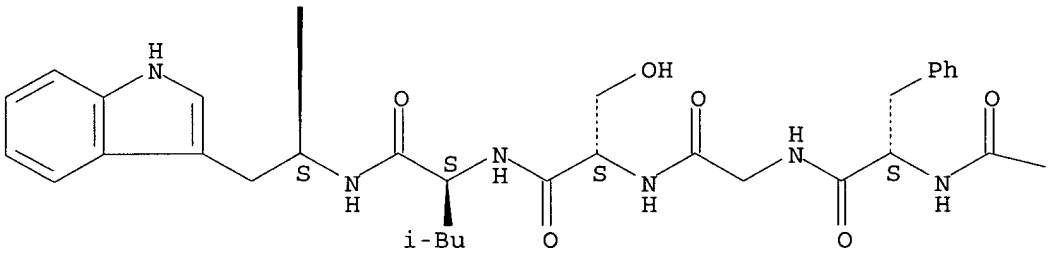

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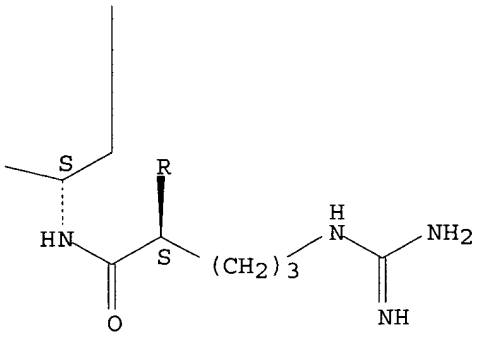

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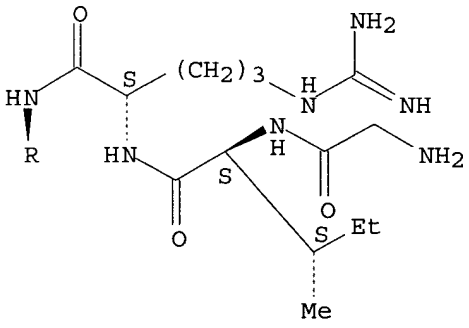

RN 697228-11-8 CAPLUS
CN L-Arginine, glycyl-L-phenylalanyl-L-arginyl-L-arginyl-L-leucyl-L-tyrosylglycyl-L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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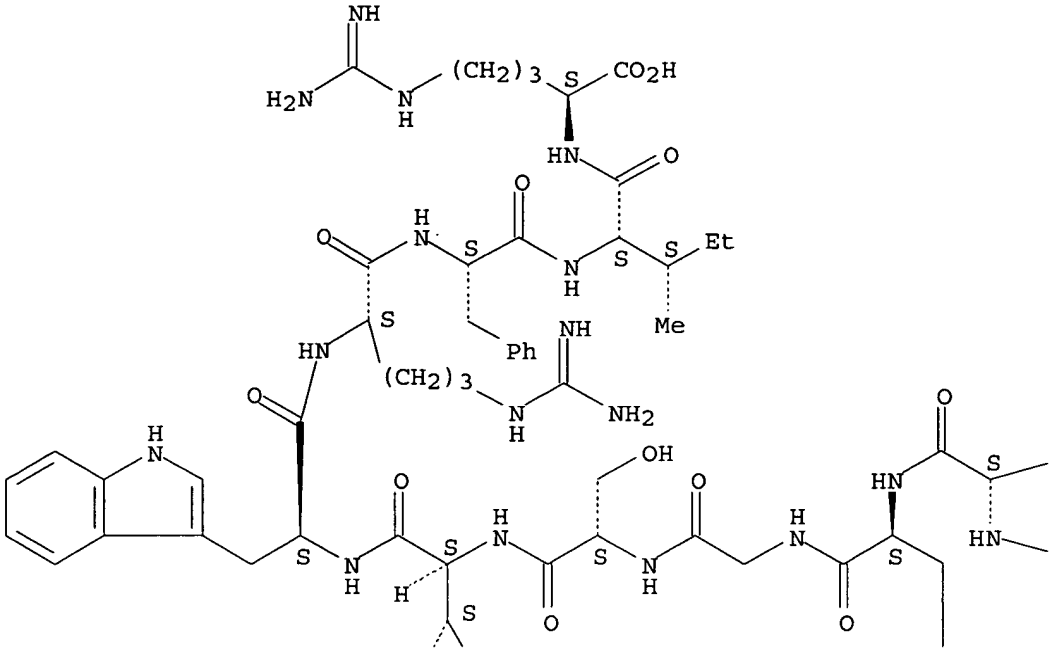

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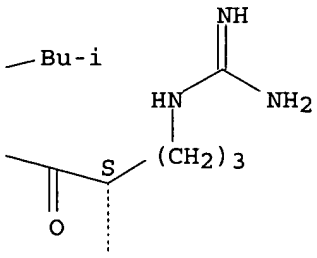
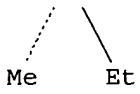
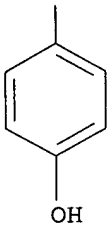
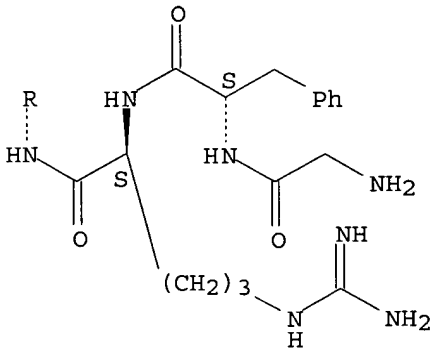


PAGE 2-A





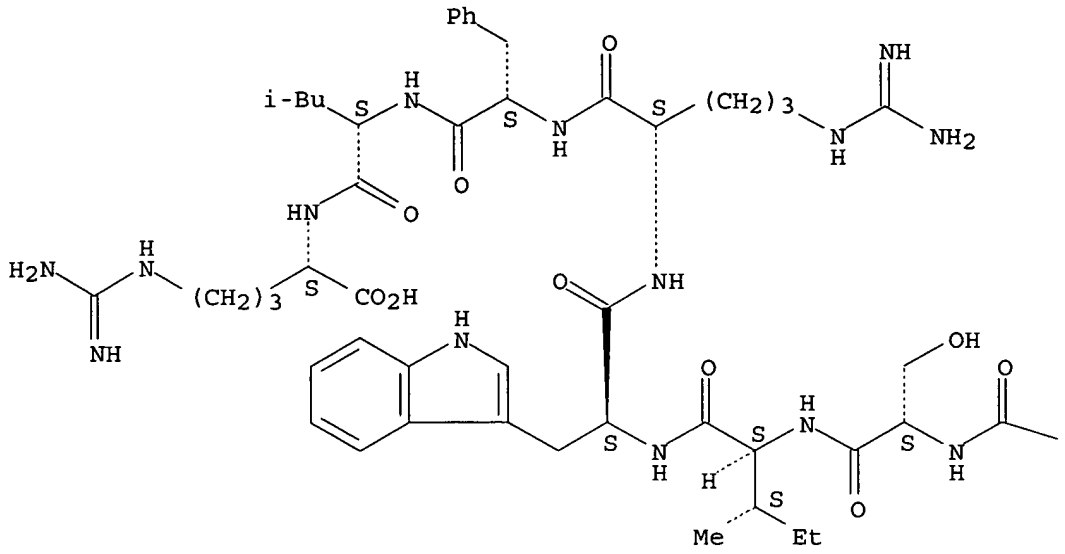


PAGE 2-B

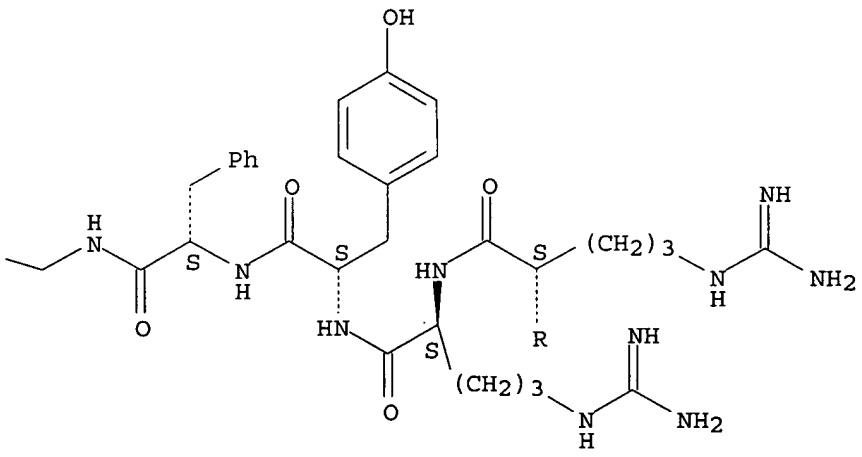
RN 697228-37-8 CAPLUS
CN L-Arginine, glycyl-L-leucyl-L-arginyl-L-arginyl-L-tyrosyl-L-phenylalanylglycyl-L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

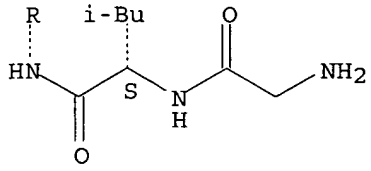
PAGE 1-A



PAGE 1-B



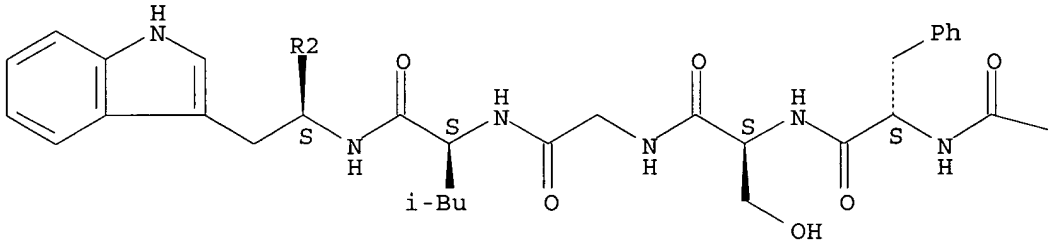
PAGE 2-A



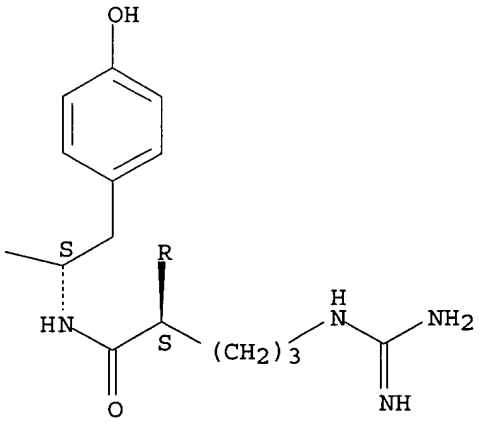
RN 697228-38-9 CAPLUS
CN L-Arginine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-tyrosyl-L-phenylalanyl-L-serylglycyl-L-leucyl-L-tryptophyl-L-arginyl-L-phenylalanyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

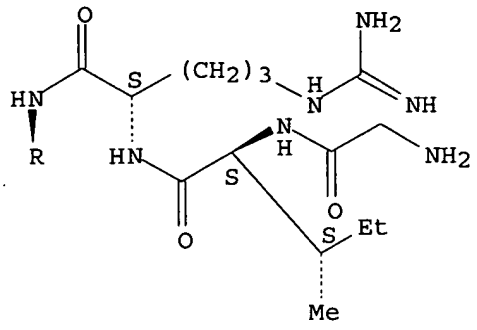
PAGE 1-A



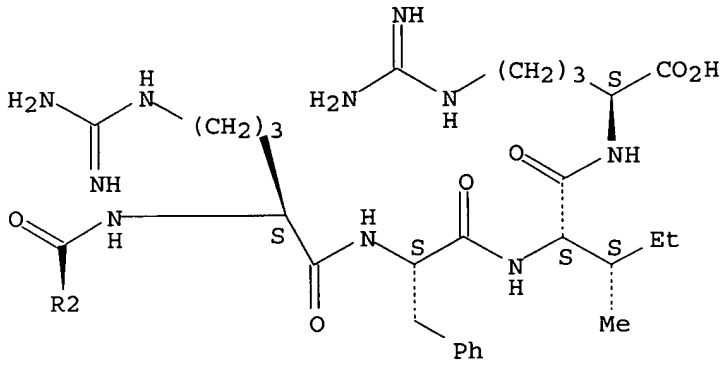
PAGE 1-B



PAGE 2-A



PAGE 3-A



RN 697228-42-5 CAPLUS
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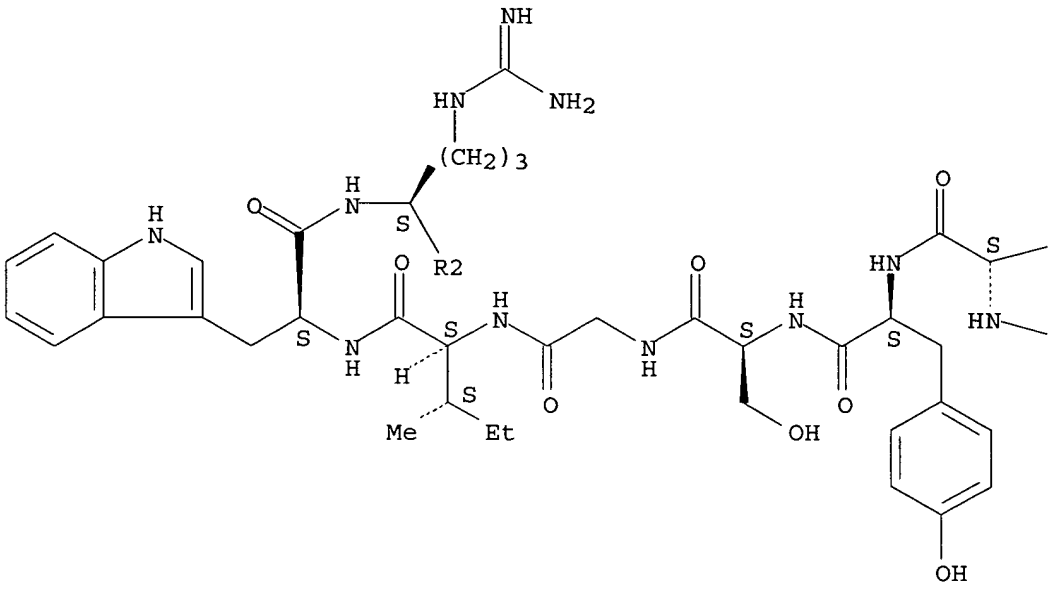
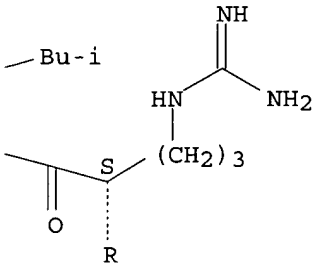
Absolute stereochemistry.

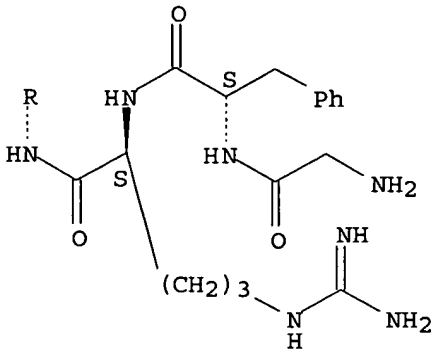
PAGE 1-A



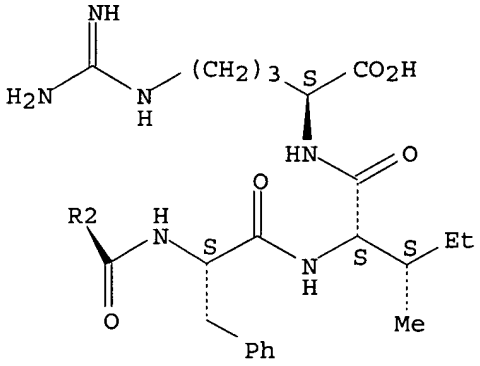
PAGE 1-B



PAGE 2-A



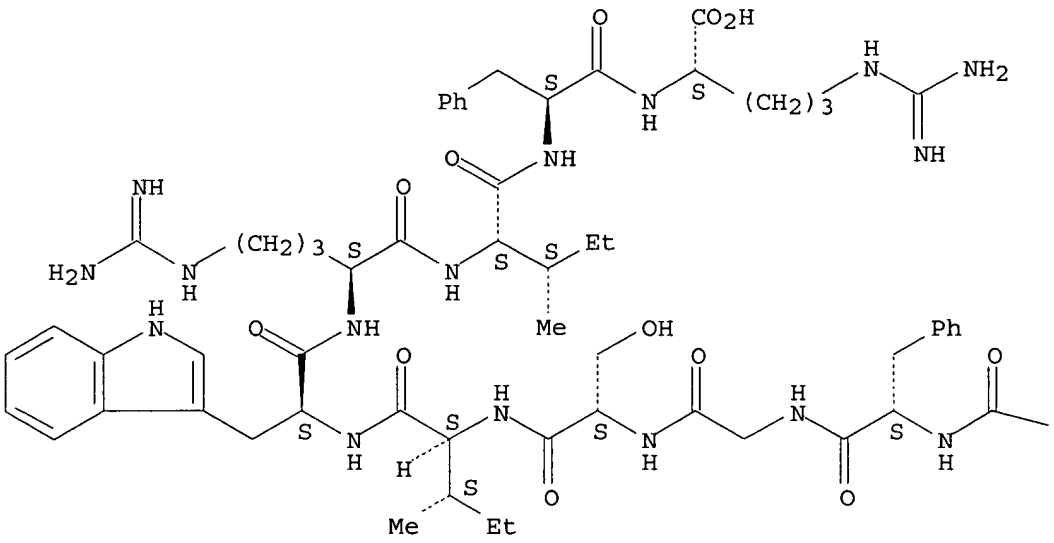
PAGE 3-A



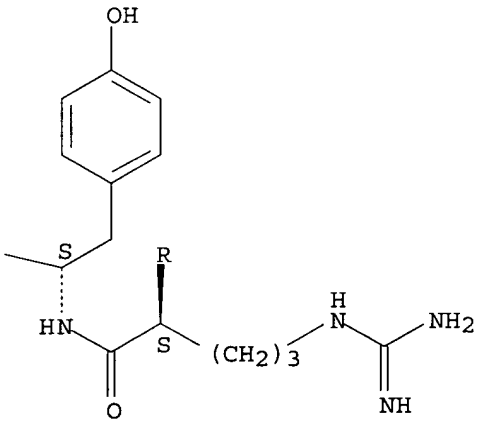
RN 697228-43-6 CAPLUS
CN L-Arginine, glycyl-L-isoleucyl-L-arginyl-L-arginyl-L-tyrosyl-L-phenylalanylglycyl-L-seryl-L-isoleucyl-L-tryptophyl-L-arginyl-L-isoleucyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

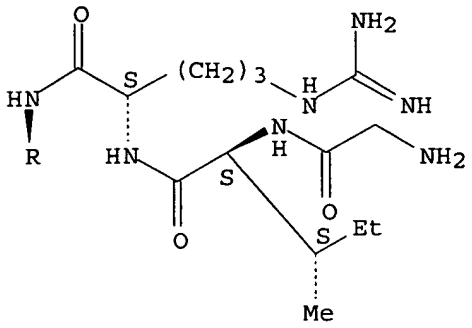
PAGE 1-A



PAGE 1-B



PAGE 2-A



=> D .CA L84 1-19

L84 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:863754 CAPLUS
DOCUMENT NUMBER: 143:339259
TITLE: An Oral ApoJ **Peptide** Renders HDL Antiinflammatory in Mice and Monkeys and Dramatically Reduces Atherosclerosis in **Apolipoprotein** E-Null Mice
AUTHOR(S): Navab, Mohamad; Anantharamaiah, G. M.; Reddy, Srinivasa T.; Van Lenten, Brian J.; Wagner, Alan C.; Hama, Susan; Bachini, Greg Hough Eugene; **Garber, David W.**; Mishra, Vinod K.; Palgunachari, Mayakonda N.; Fogelman, Alan M.
CORPORATE SOURCE: David Geffen School of Medicine at UCLA, Los Angeles, CA, USA
SOURCE: Arteriosclerosis, Thrombosis, and Vascular Biology (2005), 25(9), 1932-1937
CODEN: ATVBFA; ISSN: 1079-5642
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 23 Aug 2005
AB Objective- To determine the properties of a peptide synthesized from D-amino acids corresponding to residues 113 to 122 in apolipoprotein (apo) J. Methods and Results- In contrast to D-4F, D-[113-122]apoJ showed minimal self-association and helicity in the absence of lipids. D-4F increased the concentration of apoA-I with pre-β mobility in apoE-null mice whereas D-[113-122]apoJ did not. After an oral dose D-[113-122]apoJ more slowly associated with lipoproteins and was cleared from plasma much more slowly than D-4F. D-[113-122]apoJ significantly improved the ability of plasma to promote cholesterol efflux and improved high-d. lipoprotein (HDL) inflammatory properties for ≤48 h after a single oral dose in apoE-null mice, whereas scrambled D-[113-122]apoJ did not. Oral administration of 125 μg/mouse/d of D-[113-122]apoJ reduced atherosclerosis in apoE-null mice (70.2% reduction in aortic root sinus lesion area, +10-13; 70.5% reduction by en face anal., +10-6). In monkeys, oral D-[113-122]apoJ rapidly reduced lipoprotein lipid hydroperoxides (LOOH) and improved HDL inflammatory properties. Adding 250 ng/mL of D-[113-122]apoJ (but not scrambled D- [113-122]apoJ) to plasma in vitro reduced LOOH and increased paraoxonase activity.

Conclusions- Oral D-[113-122]apoJ significantly improves HDL inflammatory properties in mice and monkeys and inhibits lesion formation in apoE-null mice.

CC 1-7 (Pharmacology)

ST **apolipoprotein** J **peptide** atherosclerosis treatment HDL inflammation

IT Antiarteriosclerotics
(antiatherosclerotics; oral **apolipoprotein** J **peptide** renders HDL antiinflammatory in mice and monkeys and dramatically reduces atherosclerosis in **apolipoprotein** E-null mice)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hydroperoxides, decrease; oral **apolipoprotein** J **peptide** renders HDL antiinflammatory in mice and monkeys and dramatically reduces atherosclerosis in **apolipoprotein** E-null mice)

IT Hydroperoxides
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lipid, decrease; oral **apolipoprotein** J **peptide** renders HDL antiinflammatory in mice and monkeys and dramatically reduces atherosclerosis in **apolipoprotein** E-null mice)

IT Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(monocyte chemotactic factor, induction; oral **apolipoprotein** J **peptide** renders HDL antiinflammatory in mice and monkeys and dramatically reduces atherosclerosis in **apolipoprotein** E-null mice)

IT Atherosclerosis
(oral **apolipoprotein** J **peptide** renders HDL antiinflammatory in mice and monkeys and dramatically reduces atherosclerosis in **apolipoprotein** E-null mice)

IT Glycerides, biological studies
High-density lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(oral **apolipoprotein** J **peptide** renders HDL antiinflammatory in mice and monkeys and dramatically reduces atherosclerosis in **apolipoprotein** E-null mice)

IT 608513-82-2 608513-84-4 608513-86-6 608513-87-7 608513-89-9 608513-91-3 608513-92-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**apolipoprotein** J **peptide**; oral **apolipoprotein** J **peptide** renders HDL antiinflammatory in mice and monkeys and dramatically reduces atherosclerosis in **apolipoprotein** E-null mice)

IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(efflux; oral **apolipoprotein** J **peptide** renders HDL antiinflammatory in mice and monkeys and dramatically reduces atherosclerosis in **apolipoprotein** E-null mice)

IT 117698-12-1, Paraoxonase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(increase; oral **apolipoprotein** J **peptide** renders HDL antiinflammatory in mice and monkeys and dramatically reduces atherosclerosis in **apolipoprotein** E-null mice)

IT 595579-88-7, D 4F
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral **apolipoprotein** J **peptide** renders HDL

antiinflammatory in mice and monkeys and dramatically reduces atherosclerosis in **apolipoprotein** E-null mice)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:673655 CAPLUS
DOCUMENT NUMBER: 143:278780
TITLE: Inhibition of Lipopolysaccharide-Induced Inflammatory Responses by an **Apolipoprotein** AI Mimetic **Peptide**
AUTHOR(S): Gupta, Himanshu; Dai, Lijun; **Datta, Geeta**; **Garber, David W.**; Grenett, Hernan; Li, Yanbing; Mishra, Vinod; Palgunachari, Mayakonda N.; Handattu, Shaila; Gianturco, Sandra H.; Bradley, William A.; Anantharamaiah, G. M.; White, C. Roger
CORPORATE SOURCE: Department of Medicine, Division of Cardiovascular Disease, the Vascular Biology and Hypertension Program, Atherosclerosis Research Unit, University of Alabama, Birmingham, AL, USA
SOURCE: Circulation Research (2005), 97(3), 236-243
CODEN: CIRUAL; ISSN: 0009-7330
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 31 Jul 2005
AB Previous studies suggest that high-d. lipoprotein and apoAI inhibit lipopolysaccharide (LPS)-induced inflammatory responses. The goal of the current study was to test the hypothesis that the apoAI mimetic peptide L-4F exerts antiinflammatory effects similar to apoAI. Pretreatment of human umbilical vein endothelial cells (HUVECs) with LPS induced the adhesion of THP-1 monocytes. Incubation of cells with LPS and L-4F (1 to 50 μg/mL) reduced THP-1 adhesion in a concentration-dependent manner. This response was associated with a significant reduction in the synthesis of cytokines, chemokines, and adhesion mols. L-4F reduced vascular cell adhesion mol.-1 expression induced by LPS or lipid A, whereas a control peptide (Sc-4F) showed no effect. In contrast to LPS treatment, L-4F did not inhibit IL-1β- or tumor necrosis factor-α-induced vascular cell adhesion mol.-1 expression. The inhibitory effect of L-4F on LPS induction of inflammatory markers was associated with reduced binding of LPS to its plasma carrier mol., lipopolysaccharide binding protein, and decreased binding of LPS to HUVEC monolayers. LPS and L-4F in HUVEC culture medium were fractionated by fast protein liquid chromatog. and were localized to the same fractions, suggesting a phys. interaction between these mols. Proinflammatory responses to LPS are associated with the binding of lipid A to cell surface receptors. The current studies demonstrate that L-4F reduces the expression of inflammatory markers induced by LPS and lipid A and suggest that apoAI peptide mimetics may be useful in the treatment of inflammation associated with endotoxemia.
CC 1-7 (Pharmacology)
ST antiinflammatory **apolipoprotein** AI mimetic **peptide** L4F inflammatory response inhibition
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:530109 CAPLUS

DOCUMENT NUMBER: 143:222123
TITLE: D-4F and Statins Synergize to Render HDL Antiinflammatory in Mice and Monkeys and Cause Lesion Regression in Old **Apolipoprotein** E-Null Mice
AUTHOR(S): Navab, Mohamad; Anantharamaiah, G. M.; Hama, Susan; Hough, Greg; Reddy, Srinivasa T.; Frank, Joy S.; **Garber, David W.**; Handattu, Shaila; Fogelman, Alan M.
CORPORATE SOURCE: David Geffen School of Medicine, University of California, Los Angeles, CA, 90095-1679, USA
SOURCE: Arteriosclerosis, Thrombosis, and Vascular Biology (2005), 25(7), 1426-1432
CODEN: ATVBFA; ISSN: 1079-5642
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 20 Jun 2005
AB The authors tested for synergy between pravastatin and D-4F by administering oral doses of each in combination that were predetd. to be ineffective when given as single agents. The combination significantly increased high-d. lipoprotein (HDL)-cholesterol levels, apolipoprotein (apo)A-I levels, paraoxonase activity, rendered HDL antiinflammatory, prevented lesion formation in young (79% reduction in en face lesion area) and caused regression of established lesions in old apoE null mice ie, mice receiving the combination for 6 mo had lesion areas that were smaller than those before the start of treatment ($P = 0.019$ for en face lesion area; $P = 0.004$ for aortic root sinus lesion area). After 6 mo of treatment with the combination, en face lesion area was 38% of that in mice maintained on chow alone; $P < 0.00004$ with a 22% reduction in macrophage content in the remaining lesions ($P = 0.001$), indicating an overall reduction in macrophages of 79%. The combination increased intestinal apoA-I synthesis by 60%. In monkeys, the combination also rendered HDL antiinflammatory. These results suggest that the combination of a statin and an HDL-based therapy may be a particularly potent treatment strategy.
CC 1-8 (Pharmacology)
ST **apolipoprotein** A1 mimetic **peptide** pravastatin HDL antiatherosclerotic
IT **Apolipoproteins**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A-I; synergy between D-4F and statins to render HDL antiinflammatory in mice and monkeys)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:530093 CAPLUS
DOCUMENT NUMBER: 143:241146
TITLE: **Apolipoprotein** A-I Mimetic **Peptides**
AUTHOR(S): Navab, Mohamad; Anantharamaiah, G. M.; Reddy, Srinivasa T.; Hama, Susan; Hough, Greg; Grijalva, Victor R.; Yu, Nicholas; Ansell, Benjamin J.; **Datta, Geeta; Garber, David W.**; Fogelman, Alan M.
CORPORATE SOURCE: David Geffen School of Medicine at UCLA, Los Angeles, CA, 90095-1679, USA
SOURCE: Arteriosclerosis, Thrombosis, and Vascular Biology (2005), 25(7), 1325-1331
CODEN: ATVBFA; ISSN: 1079-5642
PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 20 Jun 2005
AB A review. Despite identical amino acid composition, differences in class A amphipathic helical peptides caused by differences in the order of amino acids on the hydrophobic face results in substantial differences in antiinflammatory properties. One of these peptides is an apolipoprotein A-I (apoA-I) mimetic, D-4F. When given orally to mice and monkeys, D-4F caused the formation of pre-β high-d. lipoprotein (HDL), improved HDL-mediated cholesterol efflux, reduced lipoprotein lipid hydroperoxides, increased paraoxonase activity, and converted HDL from pro-inflammatory to antiinflammatory. In apolipoprotein E (apoE)-null mice, D-4F increased reverse cholesterol transport from macrophages. Oral D-4F reduced atherosclerosis in apoE-null and low-d. lipoprotein (LDL) receptor-null mice. In vitro when added to human plasma at nanomolar concns., D-4F caused the formation of pre-β HDL, reduced lipoprotein lipid hydroperoxides, increased paraoxonase activity, and converted HDL from pro-inflammatory to antiinflammatory. Phys.-chemical properties and the ability of various class A amphipathic helical peptides to activate lecithin cholesterol acyltransferase (LCAT) in vitro did not predict biol. activity in vivo. In contrast, the use of cultured human artery wall cells in evaluating these peptides was more predictive of their efficacy in vivo. We conclude that the antiinflammatory properties of different class A amphipathic helical peptides depends on subtle differences in the configuration of the hydrophobic face of the peptides, which dets. the ability of the peptides to sequester inflammatory lipids. These differences appear to be too subtle to predict efficacy based on phys.-chemical properties alone. However, understanding these phys.-chemical properties provides an explanation for the mechanism of action of the active peptides.
CC 1-0 (Pharmacology)
ST review antiatherosclerotics **apolipoprotein** AI mimetic **peptide** D4F atherosclerosis
IT **Apolipoproteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A-I; **apolipoprotein** A-I mimetic **peptides**)
IT Antiarteriosclerotics
(antiatherosclerotics; **apolipoprotein** A-I mimetic **peptides**)
IT Atherosclerosis
Human
(**apolipoprotein** A-I mimetic **peptides**)
IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**apolipoprotein** A-I mimetic **peptides**)
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:484593 CAPLUS
DOCUMENT NUMBER: 143:379525
TITLE: **Apolipoprotein** E mimetic **peptide** dramatically lowers plasma cholesterol and restores endothelial function in Watanabe heritable hyperlipidemic rabbits
AUTHOR(S): Gupta, Himanshu; White, C. Roger; Handattu, Shaila; **Garber, David W.**; **Datta, Geeta**; Chaddha, Manjula; Dai, Lijun; Gianturco, Sandra H.; Bradley, William A.; Anantharamaiah, G. M.
CORPORATE SOURCE: Departments of Medicine, Biochemistry, and Molecular

Genetics and the Atherosclerosis Research Unit, University of Alabama at Birmingham, USA
SOURCE: Circulation (2005), 111(23), 3112-3118
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 08 Jun 2005

AB These studies were designed to determine whether the dual-domain peptide with a class A amphipathic helix linked to the receptor-binding domain of apolipoprotein (apo) E (Ac-hE-18A-NH2) possesses both antidyslipidemic and antiinflammatory properties. A single bolus (15 mg/kg IV) of Ac-hE-18A-NH2 that contains LRKLRKRLLR (141- to 150-residue region of apo E) covalently linked to apo A-I mimetic peptide 18A not only reduced plasma cholesterol levels (baseline, 562±29.0 mg/dL vs. 287.7±22.0 mg/dL at 18 h, P<0.001) in the Watanabe heritable hyperlipidemic rabbit model but also significantly improved arterial endothelial function. This improvement was associated with a reduction in 2 markers of oxidative stress. First, the plasma lipid hydroperoxide content was reduced significantly, an effect associated with a 5-fold increase in HDL paraoxonase activity. Second, the formation of superoxide anion, a scavenger of nitric oxide, was also significantly reduced in arteries of these animals. Because dyslipidemia and endothelial dysfunction are common features of the atherosclerotic disease process, this unique dual-domain peptide has ideal composite properties that ameliorate key contributory factors to atherosclerosis.

CC 1-10 (Pharmacology)

ST **apolipoprotein** E mimetic **peptide** cholesterol endothelial function hyperlipidemia

IT **Apolipoproteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(E; **apolipoprotein**-E mimetic **peptide** Ac-hE-18A-NH2 reduced plasma cholesterol, lipid hydroperoxide, superoxide anion level, increased HDL paraoxonase activity and improved endothelial function in Watanabe heritable hyperlipidemic rabbit)

IT Antiarteriosclerotics
(antiatherosclerotics; **apolipoprotein**-E mimetic **peptide** Ac-hE-18A-NH2 reduced plasma cholesterol, lipid hydroperoxide, superoxide anion level, increased HDL paraoxonase activity and improved endothelial function in Watanabe heritable hyperlipidemic rabbit)

IT Anticholesteremic agents
Atherosclerosis
Oxidative stress, biological
(**apolipoprotein**-E mimetic **peptide** Ac-hE-18A-NH2 reduced plasma cholesterol, lipid hydroperoxide, superoxide anion level, increased HDL paraoxonase activity and improved endothelial function in Watanabe heritable hyperlipidemic rabbit)

IT High-density lipoproteins
Hyperlipidemia
Low-density lipoproteins
Very-low-density lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**apolipoprotein**-E mimetic **peptide** Ac-hE-18A-NH2 reduced plasma cholesterol, lipid hydroperoxide, superoxide anion level, increased HDL paraoxonase activity and improved endothelial function in Watanabe heritable hyperlipidemic rabbit)

IT Blood vessel, disease
(endothelium; **apolipoprotein**-E mimetic **peptide** Ac-hE-18A-NH2 reduced plasma cholesterol, lipid hydroperoxide,

superoxide anion level, increased HDL paraoxonase activity and improved endothelial function in Watanabe heritable hyperlipidemic rabbit)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hydroperoxides; **apolipoprotein**-E mimetic **peptide** Ac-hE-18A-NH2 reduced plasma lipid hydroperoxide activity in Watanabe heritable hyperlipidemic rabbit)

IT Hydroperoxides
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lipid; **apolipoprotein**-E mimetic **peptide** Ac-hE-18A-NH2 reduced plasma lipid hydroperoxide activity in Watanabe heritable hyperlipidemic rabbit)

IT Endothelium
(vascular, disease; **apolipoprotein**-E mimetic **peptide** Ac-hE-18A-NH2 reduced plasma cholesterol, lipid hydroperoxide, superoxide anion level, increased HDL paraoxonase activity and improved endothelial function in Watanabe heritable hyperlipidemic rabbit)

IT 117698-12-1, Paraoxonase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**apolipoprotein**-E mimetic **peptide** Ac-hE-18A-NH2 increased high d. lipoprotein paraoxonase activity in Watanabe heritable hyperlipidemic rabbit)

IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**apolipoprotein**-E mimetic **peptide** Ac-hE-18A-NH2 reduced plasma cholesterol level in Watanabe heritable hyperlipidemic rabbit)

IT 143870-59-1 866509-52-6
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**apolipoprotein**-E mimetic **peptide** Ac-hE-18A-NH2 reduced plasma cholesterol, lipid hydroperoxide, superoxide anion level, increased HDL paraoxonase activity and improved endothelial function in Watanabe heritable hyperlipidemic rabbit)

IT 11062-77-4, Superoxide anion
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**apolipoprotein**-E mimetic **peptide** Ac-hE-18A-NH2 reduced superoxide anion levels in Watanabe heritable hyperlipidemic rabbit)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1029120 CAPLUS
DOCUMENT NUMBER: 142:129428
TITLE: Two Homologous **Apolipoprotein** AI Mimetic **Peptides**: Relationship between membrane interactions and biological activity
AUTHOR(S): Epand, Richard M.; Epand, Raquel F.; Sayer, Brian G.; **Datta, Geeta**; Chaddha, Manjula; Anantharamaiah, G. M.
CORPORATE SOURCE: Departments of Biochemistry and Biomedical Sciences and Chemistry, McMaster University, Hamilton, ON, L8N 3Z5, Can.
SOURCE: Journal of Biological Chemistry (2004), 279(49), 51404-51414
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal

LANGUAGE: English
ED Entered STN: 01 Dec 2004
AB Two related 18-amino acid, class A, amphipathic helical peptides termed 3F-2 and 3F14 were chosen for this study. Although they have identical amino acid compns. and many similar biophys. properties, 3F-2 is more potent than 3F14 as an apolipoprotein AI mimetic peptide. The two peptides exhibit similar gross conformational properties, forming structures of high helical content on a membrane surface. However, the thermal denaturation transition of 3F-2 is more cooperative, suggesting a higher degree of oligomerization on the membrane. Both 3F-2 and 3F14 promote the segregation of cholesterol in membranes containing phosphatidylcholine and cholesterol, but 3F-2 exhibits a greater selectivity for partitioning into cholesterol-depleted regions of the membrane. Magic angle spinning/NMR studies indicate that the aromatic residues of 3F-2 are stacked in the presence of lipid. The aromatic side chains of this peptide also penetrate more deeply into membranes of phosphatidylcholine with cholesterol compared with 3F14. Using the fluorescent probe, 1,3-dipyrenylpropane, the authors monitored the properties of the lipid hydrocarbon environment. 3F-2 had a greater effect in altering the properties of the hydrocarbon region of the membrane. The results are consistent with the authors' proposed model of the effect of peptide shape on the nature of the difference in peptide insertion into the bilayer.
CC 6-6 (General Biochemistry)
ST **apolipoprotein** AI mimetic **peptide** cholesterol phosphatidylcholine membrane
IT **Apolipoproteins**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)
(A-I; homologous **apolipoprotein** AI mimetic **peptides** interaction with cholesterol-phosphatidylcholine membranes)
IT Phosphatidylcholines, biological studies
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)
(bilayer membranes containing cholesterol and; homologous **apolipoprotein** AI mimetic **peptides** interaction with cholesterol-phosphatidylcholine membranes)
IT Membrane, biological
(bilayer; homologous **apolipoprotein** AI mimetic **peptides** interaction with cholesterol-phosphatidylcholine membranes)
IT Conformation
Cooperative phenomena
Denaturation
(homologous **apolipoprotein** AI mimetic **peptides** interaction with cholesterol-phosphatidylcholine membranes)
IT 26853-31-6, POPC 56421-10-4, SOPC
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)
(bilayer membranes containing cholesterol and; homologous **apolipoprotein** AI mimetic **peptides** interaction with cholesterol-phosphatidylcholine membranes)
IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)
(bilayer membranes containing phosphatidylcholine and; homologous

apolipoprotein AI mimetic **peptides** interaction with cholesterol-phosphatidylcholine membranes)

IT 388566-96-9 500759-92-2
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)
(homologous **apolipoprotein** AI mimetic **peptides** interaction with cholesterol-phosphatidylcholine membranes)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:927576 CAPLUS
DOCUMENT NUMBER: 142:16096
TITLE: Human **apolipoprotein** A-I and A-I mimetic **peptides**: potential for atherosclerosis reversal
AUTHOR(S): Navab, Mohamad; Anantharamaiah, G. M.; Reddy, Srinivasa T.; Van Lenten, Brian J.; **Datta, Geeta**; **Garber, David**; Fogelman, Alan M.
CORPORATE SOURCE: David Geffen School of Medicine, UCLA, Los Angeles, CA, USA
SOURCE: Current Opinion in Lipidology (2004), 15(6), 645-649
CODEN: COPLEU; ISSN: 0957-9672
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 04 Nov 2004
AB A review. Recent publications related to the potential use of apolipoprotein (apo)A-I and apoA-I mimetic peptides in the treatment of atherosclerosis are reviewed. A preliminary report indicating that infusion of apoA-IMilano into humans once weekly for 5 wk caused a significant decrease in coronary artery atheroma volume has sparked great interest in the potential therapeutic use of apoA-I. Recent studies have revealed that HDL quality (e.g. HDL apolipoprotein and lipid content, including oxidized lipids, particle size and electrophoretic mobility, associated enzymic activities, inflammatory/anti-inflammatory properties, and ability to promote cholesterol efflux) may be more important than HDL-cholesterol levels. Therefore, when developing new strategies to raise HDL-cholesterol concns. by interfering with HDL metabolism, one must consider the quality of the resulting HDL. In animal models, raising HDL-cholesterol levels by administering oral phospholipids improved both the quantity and quality of HDL and was associated with lesion regression. An apoA-I mimetic peptide, namely 4F synthesized from D-amino acids (D-4F), administered orally to mice did not raise HDL-cholesterol concns. but promoted the formation of pre-β HDL containing increased paraoxonase activity, resulting in significant improvements in HDL's antiinflammatory properties and ability to promote cholesterol efflux from macrophages in vitro. Oral D-4F also promoted reverse cholesterol efflux from macrophages in vivo. The quality of HDL may be more important than HDL-cholesterol levels. ApoA-I and apoA-I mimetic peptides appear to have significant therapeutic potential in atherosclerosis.
CC 1-0 (Pharmacology)
ST review **apolipoprotein** AI mimetic **peptide** antiatherosclerotic HDL cholesterol atherosclerosis
IT **Apolipoproteins**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A-I; potential of human **apolipoprotein** A-I and A-I mimetic **peptides** for atherosclerosis reversal)

IT Antiarteriosclerotics
(antiatherosclerotics; potential of human **apolipoprotein** A-I and A-I mimetic **peptides** for atherosclerosis reversal)
IT Biological transport
(efflux; potential of human **apolipoprotein** A-I and A-I mimetic **peptides** for atherosclerosis reversal)
IT Anti-inflammatory agents
Atherosclerosis
Human
(potential of human **apolipoprotein** A-I and A-I mimetic **peptides** for atherosclerosis reversal)
IT High-density lipoproteins
Phospholipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(potential of human **apolipoprotein** A-I and A-I mimetic **peptides** for atherosclerosis reversal)
IT 57-88-5, Cholesterol, biological studies 117698-12-1, Paraoxonase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(potential of human **apolipoprotein** A-I and A-I mimetic **peptides** for atherosclerosis reversal)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:835971 CAPLUS
DOCUMENT NUMBER: 142:3788
TITLE: Model class A and class L **peptides** increase the production of apoA-I-containing lipoproteins in HepG2 cells
AUTHOR(S): Dashti, Nassrin; **Datta, Geeta**; Manchekar, Medha; Chaddha, Manjula; Anantharamaiah, G. M.
CORPORATE SOURCE: Department of Medicine, Biochemistry, and Molecular Genetics, and Atherosclerosis Research Unit, University of Alabama at Birmingham, Birmingham, AL, 35294, USA
SOURCE: Journal of Lipid Research (2004), 45(10), 1919-1928
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: American Society for Biochemistry and Molecular Biology, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 13 Oct 2004
AB Class A peptides inhibit atherosclerosis and protect cells from class L peptide-mediated lysis. Because the cytolytic process is concentration dependent, we hypothesized that at certain concns. both classes of peptides exert similar effect(s) on cells. To test this hypothesis, we studied the effects of a class L peptide (18L = GIKKFLGSIWKFIKAFVG) and a class A peptide, 18A-Pro-18A (18A = DWLKAFYDKVAEKLKEAF) (37pA), on apolipoprotein and lipoprotein production in HepG2 cells. Secretion of 35S-labeled apolipoprotein A-I (apoA-I) was stimulated by both 18L (110%) and 37pA (135%) at 10 and 20 nM of peptides, resp. Both peptides enhanced the secretion of 3H-labeled phospholipids by 140% and 14C-labeled HDL-cholesterol (HDL-C) by 35% but had no significant effect on the total cholesterol mass or secretion. These results indicate that class L and class A peptides cause redistribution of cholesterol among lipoproteins in favor of HDL-C. Both peptides remodeled apoA-I-containing particles forming preβ- as well as α-HDL. This study suggests that increased secretion of phospholipids and apoA-I and the formation of preβ-HDL particles might contribute to the antiatherogenic properties of these peptides.

CC 13-2 (Mammalian Biochemistry)
Section cross-reference(s): 6
ST **peptide** apoAI HDL cholesterol lipoprotein HepG2 cell human
IT **Apolipoproteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A-I; model class A and class L **peptides** increase the production of apoA-I-containing lipoproteins in HepG2 cells)
IT High-density lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HDLc; class L and class A **peptides** cause redistribution of cholesterol among lipoproteins in favor of HDL-C)
IT Lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(high-d., **apolipoprotein** A-I-containing; model class A and class L **peptides** increase the production of apoA-I-containing lipoproteins in HepG2 cells)
IT Human
(model class A and class L **peptides** increase the production of apoA-I-containing lipoproteins in HepG2 cells)
IT **Peptides**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(model class A and class L **peptides** increase the production of apoA-I-containing lipoproteins in HepG2 cells)
IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(class L and class A **peptides** cause redistribution of cholesterol among lipoproteins in favor of HDL-C)
IT 149865-74-7 791645-03-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(model class A and class L **peptides** increase the production of apoA-I-containing lipoproteins in HepG2 cells)
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:481344 CAPLUS
DOCUMENT NUMBER: 141:201898
TITLE: Aromatic Residue Position on the Nonpolar Face of Class A Amphipathic Helical **Peptides** Determines Biological Activity
AUTHOR(S): **Datta, Geeta**; Epand, Raquel F.; Epand, Richard M.; Chaddha, Manjula; Kirksey, Matthew A.; **Garber, David W.**; Lund-Katz, Sissel; Phillips, Michael C.; Hama, Susan; Navab, Mohamad; Fogelman, Alan M.; Palgunachari, Mayakonda N.; Segrest, Jere P.; Anantharamaiah, G. M.
CORPORATE SOURCE: Departments of Medicine, Biochemistry and Molecular Genetics and the Atherosclerosis Research Unit, University of Alabama at Birmingham, Birmingham, AL, 35294, USA
SOURCE: Journal of Biological Chemistry (2004), 279(25), 26509-26517
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 15 Jun 2004
AB The apolipoprotein A-I mimetic peptide 4F (Ac-DWFKAFYDKVAEKFKEAF-NH2), with four Phe residues on the nonpolar face of the amphipathic

α-helix, is strongly anti-inflammatory, whereas two 3F analogs (3F3 and 3F14) are not. To understand how changes in helix nonpolar face structure affect function, two addnl. 3F analogs, Ac-DKLKAFYDKVFEWAKEAF-NH2 (3F-1) and Ac-DKWKAVYDKFAEAFKEFL-NH2 (3F-2), were designed using the same amino acid composition as 3F3 and 3F14. The aromatic residues in 3F-1 and 3F-2 are near the polar-nonpolar interface and at the center of the nonpolar face of the helix, resp. Like 4F, but in contrast to 3F3 and 3F14, these peptides effectively inhibited lytic peptide-induced hemolysis, oxidized phospholipid-induced monocyte chemotaxis, and scavenged lipid hydroperoxides from low d. lipoprotein. High pressure liquid chromatog. retention times and monolayer exclusion pressures indicated that there is no direct correlation of peptide function with lipid affinity. Fluorescence studies suggested that, although the peptides bind phospholipids similarly, the Trp residue in 4F, 3F-1, and 3F-2 is less motionally restricted than in 3F3 and 3F14. Based on these results and mol. modeling studies, we propose that the arrangement of aromatic residues in class A amphipathic helical mols. regulates entry of reactive oxygen species into peptide-phospholipid complexes, thereby reducing the extent of monocyte chemotaxis, an important step in atherosclerosis.

CC 6-3 (General Biochemistry)
Section cross-reference(s): 1, 15

ST **apolipoprotein** AI **peptide** activity phenylalanine atherosclerosis inflammation

IT **Apolipoproteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A-I; aromatic residue position on nonpolar face of class A amphipathic helical **peptides** dets. biol. activity)

IT Anti-inflammatory agents
Atherosclerosis
Erythrocyte
Hemolysis
Human
(aromatic residue position on nonpolar face of class A amphipathic helical **peptides** dets. biol. activity)

IT Low-density lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(aromatic residue position on nonpolar face of class A amphipathic helical **peptides** dets. biol. activity)

IT Conformation
(protein; aromatic residue position on nonpolar face of class A amphipathic helical **peptides** dets. biol. activity)

IT Hydroperoxides
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(removal; aromatic residue position on nonpolar face of class A amphipathic helical **peptides** dets. biol. activity)

IT 63-91-2, L-Phenylalanine, biological studies 143870-59-1 388566-95-8 388566-96-9 388566-97-0 500759-91-1 500759-92-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(aromatic residue position on nonpolar face of class A amphipathic helical **peptides** dets. biol. activity)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:885125 CAPLUS
DOCUMENT NUMBER: 140:246562
TITLE: Human **apolipoprotein** AI mimetic **peptides** for the treatment of atherosclerosis

AUTHOR(S): Navab, Mohamad; Anantharamaiah, G. M.; Reddy, Srinivasa T.; Van Lenten, Brian J.; Hough, Greg; Wagner, Alan; Nakamura, Kenta; **Garber, David W.**; **Datta, Geeta**; Segrest, Jere P.; Hama, Susan; Fogelman, Alan M.
CORPORATE SOURCE: Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, 90095-1679, USA
SOURCE: Current Opinion in Investigational Drugs (Thomson Current Drugs) (2003), 4(9), 1100-1104
CODEN: COIDAZ; ISSN: 1472-4472
PUBLISHER: Thomson Current Drugs
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 Nov 2003
AB The effects of apolipoprotein (Apo) AI mimetic peptide synthesized from D- and L-amino acids on atherosclerotic lesion formation were investigated in low-d. lipoprotein (LDL) receptor-deficient mice on a Western diet and in apoE null mice. In addition, their effects on the inflammatory changes induced in LDL-receptor mice fed a Western diet following influenza A infection were studied. When apolipoprotein AI mimetic peptides synthesized from either D- or L-amino acids were administered to LDL-receptor null mice, only peptides synthesized from D-amino acids were stable in the circulation and enhanced the ability of high-d. lipoprotein (HDL) to protect LDL against oxidation Administration of the peptide D-4F to LDL-receptor null mice and apoE null mice decreased lesion size. Addnl., in LDL receptor null mice after influenza infection, D-4F treatment-increased plasma HDL levels and paraoxonase activity, and inhibited increases in LDL-cholesterol and peak levels of interleukin-6 post-infection. Injection of female mice with male macrophages, and subsequent measurement of the male 'sry' gene, revealed a marked increase in macrophage traffic into the aortic arch after infection that was prevented by administration of D-4F. This indicates that: (i) oral D-4F has powerful anti-atherosclerotic properties, and (ii) the loss of the anti-inflammatory properties of HDL after influenza infection in mice is associated with increased arterial macrophage traffic that can be prevented by administration of D-4F.
CC 1-8 (Pharmacology)
ST **apolipoprotein** AI mimetic **peptide** atherosclerosis
IT **Apolipoproteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A-I; human **apolipoprotein** AI mimetic **peptides** for treatment of atherosclerosis)
IT Antiarteriosclerotics
(antiatherosclerotics; human **apolipoprotein** AI mimetic **peptides** for treatment of atherosclerosis)
IT Atherosclerosis
Human
Inflammation
Macrophage
Oxidation
Peptidomimetics
(human **apolipoprotein** AI mimetic **peptides** for treatment of atherosclerosis)
IT High-density lipoproteins
Interleukin 6
Low-density lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(human **apolipoprotein** AI mimetic **peptides** for treatment of atherosclerosis)

IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(human **apolipoprotein** AI mimetic **peptides** for treatment of atherosclerosis)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:447780 CAPLUS
DOCUMENT NUMBER: 140:534
TITLE: Effect of an arginine-rich amphipathic helical **peptide** on plasma cholesterol in dyslipidemic mice
AUTHOR(S): **Garber, David W.**; Handattu, Shaila; Aslan, Ibrahim; **Datta, Geeta**; Chaddha, Manjula; Anantharamaiah, G. M.
CORPORATE SOURCE: Departments of Medicine, Biochemistry and Molecular Genetics, and Atherosclerosis Research Unit, The University of Alabama at Birmingham, Birmingham, AL, 35294-0012, USA
SOURCE: Atherosclerosis (Shannon, Ireland) (2003), 168(2), 229-237
CODEN: ATHSBL; ISSN: 0021-9150
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 11 Jun 2003
AB We have shown that the dual domain peptide Ac-hE18A-NH2, in which LRKLRKRLLR, (141-150 region of human apo E) covalently linked to a class A lipid-associating domain, is able to associate with apo B-containing lipoproteins and enhance their clearance both in vitro and in vivo. We present here the differential effects of this peptide on the plasma cholesterol levels in different mouse models. The peptide i.v. administered (100 μg) into C57BL/6J mice on atherogenic diet, apo E null, and apo E null/LDL-receptor (LDL-R) null double knock out mouse models, was able to rapidly reduce plasma cholesterol levels within 2 min, and the effect persisted for more than 6 h. The reduction was limited to the VLDL and IDL/LDL fractions; HDL was not reduced in any mouse model studied. However, the peptide had no effect on the plasma cholesterol levels in C57BL/6J mice on normal diet, LDL-R null mice on normal chow, and LDL-R null mice on Western diet. Administration to LDL-R null mice of 125I-labeled human lipoproteins incubated with peptide resulted in accelerated human VLDL and LDL clearance with associated increase of radioactivity in the liver. These results, coupled with our earlier in vitro observations, indicate that the Arg-rich peptide-assisted rapid clearance of plasma cholesterol in dyslipidemic mice is due to the peptide targeting apo B-48-containing atherogenic lipoproteins to the liver for increased uptake and degradation
CC 1-10 (Pharmacology)
ST arginine rich amphipathic helical **peptide** plasma cholesterol dyslipidemia
IT **Apolipoproteins**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(B-48; arginine-rich amphipathic helical **peptide** Ac-hE18A-NH2 clearance of plasma cholesterol in dyslipidemic mice via targeting apo B-48 containing atherogenic lipoproteins to the liver)
IT Lipoprotein receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LDL; effect of an arginine-rich amphipathic helical **peptide**

on plasma cholesterol in dyslipidemic mice and role of LDL receptors)
IT Human
Liver
(arginine-rich amphipathic helical **peptide** Ac-hE18A-NH2 clearance of plasma cholesterol in dyslipidemic mice via targeting apo B-48 containing atherogenic lipoproteins to the liver)
IT Anticholesteremic agents
Drug targets
(effect of an arginine-rich amphipathic helical **peptide** on plasma cholesterol in dyslipidemic mice)
IT Dyslipidemia
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effect of an arginine-rich amphipathic helical **peptide** on plasma cholesterol in dyslipidemic mice)
IT High-density lipoproteins
Low-density lipoproteins
Very-low-density lipoproteins
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of an arginine-rich amphipathic helical **peptide** on plasma cholesterol in dyslipidemic mice)
IT Lipoproteins
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intermediate-d.; effect of an arginine-rich amphipathic helical **peptide** on plasma cholesterol in dyslipidemic mice)
IT 57-88-5, Cholest-5-en-3-ol (3β)-, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood; effect of an arginine-rich amphipathic helical **peptide** on plasma cholesterol in dyslipidemic mice)
IT 627552-66-3
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of an arginine-rich amphipathic helical **peptide** on plasma cholesterol in dyslipidemic mice)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:706699 CAPLUS
DOCUMENT NUMBER: 138:66452
TITLE: Influenza Infection Promotes Macrophage Traffic Into Arteries of Mice That Is Prevented by D-4F, an **Apolipoprotein** A-I Mimetic **Peptide**
AUTHOR(S): Van Lenten, Brian J.; Wagner, Alan C.; Anantharamaiah, G. M.; **Garber, David W.**; Fishbein, Michael C.; Adhikary, Lopa; Nayak, Debi P.; Hama, Susan; Navab, Mohamad; Fogelman, Alan M.
CORPORATE SOURCE: Deo, Ned, University of California, Los Angeles, CA, USA
SOURCE: Circulation (2002), 106(9), 1127-1132
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 18 Sep 2002
AB We reported that HDL loses its antiinflammatory properties during acute influenza A infection in mice, and we hypothesized that these changes might be associated with increased trafficking of macrophages into the artery wall. The present study tested this hypothesis. D-4F, an apolipoprotein

A-I mimetic peptide, or vehicle in which it was dissolved (PBS) was administered daily to LDL receptor-null mice after a western diet and after influenza infection. D-4F treatment increased plasma HDL cholesterol and paraoxonase activity compared with PBS and inhibited increases in LDL cholesterol and peak levels of interleukin-6 after infection. Lung viral titers were reduced by 50% in mice receiving D-4F. Injection of female mice with male macrophages, which were detected with real-time polymerase chain reaction to measure the male Sry gene, revealed a marked increase in macrophage traffic into the aortic arch and innominate arteries after infection that was prevented by administration of D-4F. We conclude that loss of antiinflammatory properties of HDL after influenza infection in mice is associated with increased arterial macrophage traffic that can be prevented by administration of D-4F.

CC 1-8 (Pharmacology)
Section cross-reference(s): 15

ST **apolipoprotein peptide** D4F macrophage lipoprotein influenza infection

IT **Apolipoproteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A-I; **apolipoprotein** A-I mimetic **peptide** D-4F prevented macrophage traffic into arteries and HDL from becoming proinflammaory after influenza infection)

IT **Peptides**, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(D-4F; **apolipoprotein** A-I mimetic **peptide** D-4F prevented macrophage traffic into arteries and HDL from becoming proinflammaory after influenza infection)

IT Antiarteriosclerotics
Antiviral agents
Artery
Atherosclerosis
Cell migration
Influenza A virus
Macrophage
(**apolipoprotein** A-I mimetic **peptide** D-4F prevented macrophage traffic into arteries and HDL from becoming proinflammaory after influenza infection)

IT Interleukin 6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**apolipoprotein** A-I mimetic **peptide** D-4F prevented macrophage traffic into arteries and HDL from becoming proinflammaory after influenza infection)

IT High-density lipoproteins
Low-density lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cholesterol; **apolipoprotein** A-I mimetic **peptide** D-4F prevented macrophage traffic into arteries and HDL from becoming proinflammaory after influenza infection)

IT Inflammation
Lung, disease
(pneumonitis; **apolipoprotein** A-I mimetic **peptide** D-4F prevented macrophage traffic into arteries and HDL from becoming proinflammaory after influenza infection)

IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HDL and LDL; **apolipoprotein** A-I mimetic **peptide** D-4F prevented macrophage traffic into arteries and HDL from becoming proinflammaory after influenza infection)

IT 117698-12-1, Organophosphate esterase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**apolipoprotein** A-I mimetic **peptide** D-4F prevented macrophage traffic into arteries and HDL from becoming proinflammaory after influenza infection)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:150357 CAPLUS
DOCUMENT NUMBER: 137:195286
TITLE: Oral administration of an apo A-I mimetic **peptide** synthesized from D-amino acids dramatically reduces atherosclerosis in mice independent of plasma cholesterol
AUTHOR(S): Navab, Mohamad; Anantharamaiah, G. M.; Hama, Susan; **Garber, David W.**; Chaddha, Manjula; Hough, Greg; Lallone, Roger; Fogelman, Alan M.
CORPORATE SOURCE: Department of Medicine, University California, Los Angeles, CA, 90095-1679, USA
SOURCE: Circulation (2002), 105(3), 290-292
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 27 Feb 2002
AB When apolipoprotein A-I mimetic peptides synthesized from either D- or L-amino acids were given orally to LDL receptor-null mice, only the peptide synthesized from D-amino acids was stable in the circulation and enhanced the ability of HDL to protect LDL against oxidation The peptide synthesized from L-amino acids was rapidly degraded and excreted in the urine. When a peptide synthesized from D-amino acids (D-4F) was administered orally to LDL receptor-null mice on a Western diet, lesions decreased by 79%. When added to the drinking water of apoE-null mice, D-4F decreased lesions by approx. 75% at the lowest dose tested (0.05 mg/mL). The marked reduction in lesions occurred independent of changes in total plasma or HDL-cholesterol.
CC 1-8 (Pharmacology)
ST **apolipoprotein** A I mimetic **peptide** D amino acid antiatherosclerotic; atherosclerosis **apolipoprotein** A I mimetic **peptide** D amino acid
IT **Apolipoproteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A-I, mimetic **peptides**; oral administration of an apo A-I mimetic **peptide** synthesized from D-amino acids dramatically reduces atherosclerosis in mice independent of plasma cholesterol)
IT Antiarteriosclerotics
(antiatherosclerotics; oral administration of an apo A-I mimetic **peptide** synthesized from D-amino acids dramatically reduces atherosclerosis in mice independent of plasma cholesterol)
IT Atherosclerosis
(oral administration of an apo A-I mimetic **peptide** synthesized from D-amino acids dramatically reduces atherosclerosis in mice independent of plasma cholesterol)
IT Low-density lipoproteins
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(oral administration of an apo A-I mimetic **peptide** synthesized from D-amino acids dramatically reduces atherosclerosis in mice independent of plasma cholesterol)
IT High-density lipoproteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(oral administration of an apo A-I mimetic **peptide** synthesized from D-amino acids dramatically reduces atherosclerosis in mice independent of plasma cholesterol)

IT 452782-01-3 452782-06-8
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison; oral administration of an apo A-I mimetic **peptide** synthesized from D-amino acids dramatically reduces atherosclerosis in mice independent of plasma cholesterol)

IT 143870-59-1 388566-97-0
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral administration of an apo A-I mimetic **peptide** synthesized from D-amino acids dramatically reduces atherosclerosis in mice independent of plasma cholesterol)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:570694 CAPLUS
DOCUMENT NUMBER: 135:284581
TITLE: Toward the design of **peptide** mimics of antiatherogenic **apolipoproteins** A-I and E
AUTHOR(S): Anantharamaiah, G. M.; Datta, G.; **Garber, D. W.**
CORPORATE SOURCE: Department of Medicine, Biochemistry and Molecular Genetics, The University of Alabama at Birmingham Medical Center, Birmingham, AL, 35294, USA
SOURCE: Current Science (2001), 81(1), 53-65
CODEN: CUSCAM; ISSN: 0011-3891
PUBLISHER: Current Science Association
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 08 Aug 2001
AB A review with refs. Two major markers for atherosclerosis are increased plasma cholesterol levels and low levels of high d. lipoproteins (HDL). Human apolipoprotein (apo) A-I, the major protein component of HDL, has been shown to inhibit atherosclerosis in vivo without altering plasma cholesterol levels, perhaps through its antioxidant effect on low d. lipoproteins (LDL). On the other hand, apo E inhibits atherosclerosis by enhancing the uptake of atherogenic lipoproteins by the liver and thus lowering plasma cholesterol levels. The class A amphipathic peptide 18A and its analogs, designed based on the lipid-associating amphipathic helical motif present in apo A-I, have been shown by us to mimic properties of apo A-I. Recently, we have shown that administration of an analog of 18A was also able to inhibit atherosclerosis in atherosclerosis-sensitive mice, similar to apo A-I, without altering the plasma cholesterol levels. Based on the presence of two domains in apo E, the lipid-associating domain and the receptor-binding cationic domain, linking residues 141-150 of apo E to 18A resulted in a peptide that enhanced the uptake of atherogenic lipoproteins in vitro. Administration of this peptide into dyslipidemic mice showed a dramatic decrease in plasma cholesterol levels. These results demonstrate the potential for the design of peptides to ameliorate atherosclerosis, the number one cause of mortality in the developed countries.
CC 6-0 (General Biochemistry)
Section cross-reference(s): 1, 14
ST review **peptide** design mimic **apolipoprotein** AI E atherosclerosis
IT **Apolipoproteins**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(A-I; design of **peptide** mimics of antiatherogenic **apolipoproteins** A-I and E)

IT **Apolipoproteins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E; design of **peptide** mimics of antiatherogenic **apolipoproteins** A-I and E)

IT **Peptides**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(amphipathic **peptide** 18A and analogs; design of **peptide** mimics of antiatherogenic **apolipoproteins** A-I and E)

IT Atherosclerosis
Protein engineering
(design of **peptide** mimics of antiatherogenic **apolipoproteins** A-I and E)

IT Lipoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(high-d.; design of **peptide** mimics of antiatherogenic **apolipoproteins** A-I and E)

IT Lipoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(low-d.; design of **peptide** mimics of antiatherogenic **apolipoproteins** A-I and E)

IT Biological transport
(uptake, of atherogenic lipoproteins; design of **peptide** mimics of antiatherogenic **apolipoproteins** A-I and E)

IT 57-88-5, Cholesterol, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(design of **peptide** mimics of antiatherogenic **apolipoproteins** A-I and E)

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:413082 CAPLUS
DOCUMENT NUMBER: 135:251698
TITLE: Cationic domain 141-150 of **apoE** covalently linked to a class A amphipathic helix enhances atherogenic lipoprotein metabolism in vitro and in vivo
AUTHOR(S): **Datta, Geeta; Garber, David W.**; Chung, Byung Hong; Chaddha, Manjula; Dashti, Nassrin; Bradley, William A.; Gianturco, Sandra H.; Anantharamaiah, G. M.
CORPORATE SOURCE: Departments of Medicine, the Atherosclerosis Research Unit, University of Alabama at Birmingham Medical Center, Birmingham, AL, 35294, USA
SOURCE: Journal of Lipid Research (2001), 42(6), 959-966
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 08 Jun 2001

AB We previously showed that a peptide, Ac-hE18A-NH2, in which the arginine-rich heparin-binding domain of apolipoprotein E (apoE) [residues 141-150] (LRKLRKRLLR), covalently linked to 18A (DWLKAFYDKVAEKLKEAF; a class A amphipathic helix with high lipid affinity), enhanced LDL uptake and clearance. Because VLDL and remnants contain more cholesterol per particle than LDL, enhanced hepatic clearance of VLDL could lead to an effective lowering of plasma cholesterol. Therefore, in the present article we compared the ability of this peptide to mediate/facilitate the uptake and degradation of LDL and VLDL in HepG2 cells. The peptide Ac-hE18A-NH2, but not Ac-18A-NH2, enhanced the uptake of LDL by HepG2 cells 5-fold and its degradation 2-fold. The association of the peptides with VLDL resulted in the displacement of native apoE; however, only Ac-hE18A-NH2 but not Ac-18A-NH2 caused markedly enhanced uptake (6-fold) and degradation (3-fold) of VLDL. Ac-hE18A-NH2 also enhanced the uptake (15-fold) and degradation (2-fold) of trypsinized VLDL Sf 100-400 (containing no immunodetectable apoE), indicating that the peptide restored the cellular interaction of VLDL in the absence of its essential native ligand (apoE). Pretreatment of HepG2s with heparinase and heparitinase abrogated all peptide-mediated enhanced cellular activity, implicating a role for cell-surface heparan sulfate proteoglycans (HSPG). I.v. administration of Ac-hE18A-NH2 into apoE gene knockout mice reduced plasma cholesterol by 88% at 6 h and 30% at 24 h after injection. We conclude that this dual-domain peptide assocs. with LDL and VLDL and results in rapid hepatic uptake via a HSPG-facilitated pathway.

CC 1-8 (Pharmacology)

ST **apolipoprotein** E cationic domain fusion amphipathic helix atherogenic lipoprotein; LDL VLDL uptake clearance **apoE** fusion amphipathic helix anticholesterolemic

IT **Apolipoproteins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E, displacement from VLDL surface by dual domain **peptide**; cationic domain 141-150 of **apoE** covalently linked to a class A amphipathic helix enhances atherogenic lipoprotein metabolism in vitro and in vivo and lowers plasma cholesterol)

IT **Apolipoproteins**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E, fusion products, with amphipathic helix; cationic domain 141-150 of **apoE** covalently linked to a class A amphipathic helix enhances atherogenic lipoprotein metabolism in vitro and in vivo and lowers plasma cholesterol)

IT Anticholesteremic agents
Molecular association
(cationic domain 141-150 of **apoE** covalently linked to a class A amphipathic helix enhances atherogenic lipoprotein metabolism in vitro and in vivo and lowers plasma cholesterol)

IT Blood plasma
(cholesterol; cationic domain 141-150 of **apoE** covalently linked to a class A amphipathic helix enhances atherogenic lipoprotein metabolism in vitro and in vivo and lowers plasma cholesterol)

IT Proteoglycans, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(heparitin sulfate-containing; cationic domain 141-150 of **apoE** covalently linked to a class A amphipathic helix enhances atherogenic lipoprotein metabolism in vitro and in vivo and lowers plasma cholesterol)

IT Biological transport

(internalization, of LDL and VLDL; cationic domain 141-150 of **apoE** covalently linked to a class A amphipathic helix enhances atherogenic lipoprotein metabolism in vitro and in vivo and lowers plasma cholesterol)

IT Lipoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(low-d.; cationic domain 141-150 of **apoE** covalently linked to a class A amphipathic helix enhances atherogenic lipoprotein metabolism in vitro and in vivo and lowers plasma cholesterol)

IT Lipoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(very-low-d.; cationic domain 141-150 of **apoE** covalently linked to a class A amphipathic helix enhances atherogenic lipoprotein metabolism in vitro and in vivo and lowers plasma cholesterol)

IT 361191-16-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic domain 141-150 of **apoE** covalently linked to a class A amphipathic helix enhances atherogenic lipoprotein metabolism in vitro and in vivo and lowers plasma cholesterol)

IT 57-88-5, Cholesterol, biological studies
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(cationic domain 141-150 of **apoE** covalently linked to a class A amphipathic helix enhances atherogenic lipoprotein metabolism in vitro and in vivo and lowers plasma cholesterol)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:310178 CAPLUS
DOCUMENT NUMBER: 135:102279
TITLE: A new synthetic class A amphipathic **peptide** analogue protects mice from diet-induced atherosclerosis
AUTHOR(S): **Garber, David W.**; **Datta, Geeta**; Chaddha, Manjula; Palgunachari, M. N.; Hama, Susan Y.; Navab, Mohamad; Fogelman, Alan M.; Segrest, Jere P.; Anantharamaiah, G. M.
CORPORATE SOURCE: The Atherosclerosis Research Unit and the Departments of Medicine and Biochemistry and Molecular Genetics, The University of Alabama at Birmingham, Birmingham, AL, 35294, USA
SOURCE: Journal of Lipid Research (2001), 42(4), 545-552
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 02 May 2001
AB Several synthetic class A peptide analogs have been shown to mimic many of the properties of human apo A-I in vitro. A new peptide [acetyl-(AspTrpLeuLysAlaPheTyrAspLysValPheGluLysPheLysGluPhePhe)-NH2; 5F], with increased amphipathicity, was administered by i.p. injection, 20 μg/day for 16 wk, to C57BL/6J mice fed an atherogenic diet. Mouse apo A-I (MoA-I) (50 μg/day) or phosphate-buffered saline (PBS) injections were given to other mice as controls. Total plasma cholesterol levels and

lipoprotein profiles were not significantly different between the treated and control groups, except that the mice receiving 5F or MoA-I had lower high d. lipoprotein (HDL) cholesterol when calculated as a percentage of total cholesterol. No toxicity or production of antibodies to the injected materials was observed When HDL was isolated from high fat diet-administered mice injected with 5F and presented to human artery wall cells in vitro together with human low d. lipoprotein (LDL), there were substantially fewer lipid hydroperoxides formed and substantially less LDL-induced monocyte chemotactic activity than with HDL from PBS-injected animals. Injection of human apo A-I produced effects similar to 5F on lipid peroxide formation and LDL-induced monocyte chemotactic activity, but injection of MoA-I was significantly less effective in reducing lipid hydroperoxide formation or lowering LDL-induced monocyte chemotactic activity. Mice receiving peptide 5F had significantly less aortic atherosclerotic lesion area compared with mice receiving PBS, whereas lesion area in mice receiving MoA-I was similar to that of the PBS-injected animals. This is the first in vivo demonstration that a model class A amphipathic helical peptide has antiatherosclerotic properties. We conclude that 5F inhibits lesion formation in high fat diet-administered mice by a mechanism that does not involve changes in the lipoprotein profile, and may have potential in the prevention and treatment of atherosclerosis.

CC 1-8 (Pharmacology)

ST antiatherosclerotic **peptide** analog **apolipoprotein** A1 cholesterol HDL

IT **Apolipoproteins**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(A-I; a new amphipathic **peptide** analog protects mice from diet-induced atherosclerosis)

IT Antiarteriosclerotics
(antiatherosclerotics; a new amphipathic **peptide** analog protects mice from diet-induced atherosclerosis)

IT Lipoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(high-d.; a new amphipathic **peptide** analog protects mice from diet-induced atherosclerosis)

IT Peroxides, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(lipid; a new amphipathic **peptide** analog protects mice from diet-induced atherosclerosis)

IT Chemotaxis
(monocytes; a new amphipathic **peptide** analog protects mice from diet-induced atherosclerosis)

IT Lipids, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(peroxides; a new amphipathic **peptide** analog protects mice from diet-induced atherosclerosis)

IT 204633-67-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(a new amphipathic **peptide** analog protects mice from diet-induced atherosclerosis)

IT 57-88-5, Cholesterol, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(blood; a new amphipathic **peptide** analog protects mice from diet-induced atherosclerosis)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:894790 CAPLUS
DOCUMENT NUMBER: 134:290170
TITLE: The receptor binding domain of **apolipoprotein** E, linked to a model class A amphipathic helix, enhances internalization and degradation of LDL in fibroblasts
AUTHOR(S): Chaddha, Manjula; **Datta, Geeta**; **Garber, David W.**; Chung, Byong Hong; Tytler, Ewan M.; Bradley, William A.; Gianturco, Sandra H.; Anantharamaiah, G. M.
CORPORATE SOURCE: Department of Medicine, University of Alabama at Birmingham Medical Center, Birmingham, AL, 35294, USA
SOURCE: Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 651-652. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Kluwer Academic Publishers: Dordrecht, Neth.
CODEN: 69ATHX
DOCUMENT TYPE: Conference
LANGUAGE: English
ED Entered STN: 21 Dec 2000
AB Apolipoprotein E (apo E) plays an important role in the metabolism of triglyceride-rich lipoprotein, such as very low d. lipoprotein (VLDL) and chylomicron remnants. It mediates the high affinity binding of apo E-containing lipoproteins to the low d. lipoprotein (LDL) receptor (LDLR) and the members of its gene family, including the lipoprotein receptor related protein (LRP). Thrombin cleavage studies of lipid bound apo E suggested that it has two distinct domains, the C-terminal lipid associating domain and the N-terminal LDLR binding site (129-169). The hypothesis that a minimal arginine-rich apo E receptor binding domain (141-150) when covalently linked to a class A amphipathic helix is sufficient to enhance LDL uptake and clearance, was tested. The peptide hApoE[141-150]-18A (hE18A) and its end protected analog, Ac-hE18A-NH2, were synthesized. The importance of Lys residues and the role of the hydrophobic residues were studied using the analogs Ac-LRRLRRRLLR-NH2 (Ac-hER18A-NH2) and Ac-LRKMRKRLMR-NH2 (Ac-mE18A-NH2). These peptides show a potential for use in therapeutic intervention of atherosclerosis.
CC 1-8 (Pharmacology)
ST **apolipoprotein peptide** receptor binding LDL internalization; atherosclerosis **apolipoprotein** receptor domain LDL degrdn
IT **Apolipoproteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(E; the receptor binding domain of **apolipoprotein** E, linked to a model class A amphipathic helix, enhances internalization and degradation of LDL in fibroblasts)
IT Proteoglycans, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(heparitin sulfate-containing; the receptor binding domain of **apolipoprotein** E, linked to a model class A amphipathic helix, enhances internalization and degradation of LDL in fibroblasts)
IT Lipoproteins

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(low-d.; the receptor binding domain of **apolipoprotein** E, linked to a model class A amphipathic helix, enhances internalization and degradation of LDL in fibroblasts)

IT Endocytosis
Protein degradation
(the receptor binding domain of **apolipoprotein** E, linked to a model class A amphipathic helix, enhances internalization and degradation of LDL in fibroblasts)

IT 334686-98-5 334686-99-6 334687-00-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(the receptor binding domain of **apolipoprotein** E, linked to a model class A amphipathic helix, enhances internalization and degradation of LDL in fibroblasts)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:398895 CAPLUS
DOCUMENT NUMBER: 129:158076
TITLE: Studies of Synthetic **Peptides** of Human **Apolipoprotein** A-I Containing Tandem Amphipathic α-Helixes
AUTHOR(S): Mishra, Vinod K.; Palgunachari, Mayakonda N.; **Datta, Geeta**; Phillips, Michael C.; Lund-Katz, Sissel; Adeyeye, Samuel O.; Segrest, Jere P.; Anantharamaiah, G. M.
CORPORATE SOURCE: Departments of Medicine Biochemistry and Molecular Genetics, UAB Medical Center, Birmingham, AL, 35294, USA
SOURCE: Biochemistry (1998), 37(28), 10313-10324
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 01 Jul 1998
AB In mature human apolipoprotein A-I (apo A-I), the amino acid residues 1-43 are encoded by exon 3, whereas residues 44-243 are encoded by exon 4 of the apo A-I gene. The region encoded by exon 4 of the apo A-I gene contains 10 tandem amphipathic α-helixes; their location and the class to which they belong are as follows: helix 1 (44-65, class A1), helix 2 (66-87, class A1), helix 3 (88-98, class Y), helix 4 (99-120, class Y), helix 5 (121-142, class A1), helix 6 (143-164, class A1), helix 7 (165-186, class A1), helix 8 (187-208, class A1), helix 9 (209-219, class Y), and helix 10 (220-241, class Y). To examine the effects of multiple tandem amphipathic helixes compared to individual helixes of apo A-I on lipid association, we have studied lipid-associating properties of the following peptides: Ac-44-87-NH2 (peptide 1-2), Ac-66-98-NH2 (peptide 2-3), Ac-66-120-NH2 (peptide 2-3-4), Ac-88-120-NH2 (peptide 3-4), Ac-99-142-NH2 (peptide 4-5), Ac-121-164-NH2 (peptide 5-6), Ac-143-186-NH2 (peptide 6-7), Ac-165-208-NH2 (peptide 7-8), Ac-187-219-NH2 (peptide 8-9), and Ac-209-241-NH2 (peptide 9-10). To study lipid-associating properties of the region encoded by exon 3 of the apo A-I gene, 1-33-NH2 (peptide G*) has also been studied. The results of the present study indicate that, among the peptides studied, peptides 1-2 and 9-10 possess significantly higher lipid affinity than the other peptides, with peptide 9-10 having higher lipid affinity than peptide 1-2, as evidenced by (i) higher helical content in the presence of 1,2-dimyristoyl-sn-glycero-3-phosphocholine

(DMPC), (ii) faster rate of association with DMPC multilamellar vesicles (MLV), (iii) greater reduction in the enthalpy of gel to liquid-crystalline phase transition of DMPC MLV, (iv) higher exclusion pressure from an egg yolk phosphatidylcholine monolayer, and (v) higher partitioning into 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine MLV. A comparison of the free energies of lipid association (ΔG) of the peptides studied here with those studied previously by us [Palgunachari, M. N., et al. (1996) Arterioscler. Thromb. Vasc. Biol. 16, 328-338] indicates that, except for the peptides 4-5 and 5-6, other peptides possess higher lipid affinities compared to constituent helixes. However, the lipid affinities of the peptides studied here are neither higher than nor equal to the sum of the lipid affinities of the constituent helixes. This indicates the absence of cooperativity among the adjacent amphipathic helical domains of apo A-I for lipid association As indicated by ΔG, the lipid affinity of peptide 4-5 is higher than peptide 5 but lower than peptide 4; the lipid affinity of peptide 5-6 is lower than both peptides 5 and 6. Implications of these results for the structure and function of apo A-I are discussed.

CC 6-3 (General Biochemistry)

ST **apolipoprotein** AI tandem helix lipid affinity; phospholipid affinity **apolipoprotein** AI tandem helix

IT **Apolipoproteins**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(A-I; studies of lipid affinity of synthetic **peptides** of human **apolipoprotein** A-I containing tandem amphipathic α-helixes)

IT Membrane, biological
(bilayer; studies of lipid affinity of synthetic **peptides** of human **apolipoprotein** A-I containing tandem amphipathic α-helixes)

IT Membrane phase transition, biological
(gel-liquid crystalline; studies of lipid affinity of synthetic **peptides** of human **apolipoprotein** A-I containing tandem amphipathic α-helixes)

IT Phosphatidylcholines, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(membranes; studies of lipid affinity of synthetic **peptides** of human **apolipoprotein** A-I containing tandem amphipathic α-helixes)

IT Membrane, biological
(monolayer; studies of lipid affinity of synthetic **peptides** of human **apolipoprotein** A-I containing tandem amphipathic α-helixes)

IT Free energy of binding
Molecular association
α-Helix
(studies of lipid affinity of synthetic **peptides** of human **apolipoprotein** A-I containing tandem amphipathic α-helixes)

IT Phospholipids, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(studies of lipid affinity of synthetic **peptides** of human **apolipoprotein** A-I containing tandem amphipathic α-helixes)

IT 18194-24-6, DMPC 26853-31-6, POPC
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(membranes; studies of lipid affinity of synthetic **peptides** of human **apolipoprotein** A-I containing tandem amphipathic

α-helixes)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:631070 CAPLUS
DOCUMENT NUMBER: 117:231070
TITLE: Turnover of synthetic class A amphipathic **peptide** analogs of exchangeable **apolipoproteins** in rats. Correlation with physical properties
AUTHOR(S): **Garber, David W.**; Venkatachalapathi, Y. V.; Gupta, Kiran B.; Ibdah, Jamal; Phillips, Michael C.; Hazelrig, Jane B.; Segrest, Jere P.; Anantharamaiah, G. M.
CORPORATE SOURCE: Dep. Med., Univ. Alabama, Birmingham, AL, 35294, USA
SOURCE: Arteriosclerosis and Thrombosis (1992), 12(8), 886-94
CODEN: ARTTE5; ISSN: 1049-8834
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 13 Dec 1992
AB Peptide analogs of the class A amphipathic helixes from exchangeable apolipoproteins mimic apolipoprotein (apo) A-I in a number of ways, including the ability to activate the enzyme lecithin:cholesterol acyltransferase, to associate with HDL, and to form HDL-like particles in the presence of lipids. This study investigated the metabolic properties of several of these peptide analogs in the rat. Peptide analogs studied were L-18A (which mimics apolipoprotein amphipathic helical domains in its charge distribution), 37pA (a dimer of two 18A monomers separated by a proline), 18R (with reversed charge distribution compared with 18A), and D-18A (identical in amino acid sequence to 18A but synthesized from D-amino acids). Peptides were radiolabeled with 125I. In addition, metabolism of rat and human 125I-apo A-I and human 14C-apo A-I was studied; no significant differences in clearance of these prepns. were seen. Clearance data were fitted to multiexponential equations to give half-times of clearance; biexponential equations consistently provided the best nonlinear least-squares curve fit. The order of relative lipid affinity determined in vitro was 37pA > apo A-I > D-18A = L-18A > 18R. Half-times of clearance were in the same approx. rank order: 37pA and apo A-I, 6.9 h; D-18A, 4.0 h; L-18A, 4.6 h; and 18R, 0.9 h. Rats injected with L-18A had five times more radioactivity in the urine than did rats injected with D-18A. All urine radioactivity was present as free 125I in rats injected with L-18A or apo A-I but was present as intact peptide (with no free 125I) in rats injected with D-18A. The majority of radioactivity in L- and D-18A-injected rats was associated with the thyroid gland (in the case of L-18A), the liver, and the kidney. In summary, the rates of clearance of amphipathic helical peptides from the plasma compartment in rats decrease as the affinities of the peptides for lipoprotein surfaces increase. Stereoconformation did not affect the rate of clearance of peptide analogs. Although a significant proportion of radioactivity in L- and D-18A-injected animals was associated with the kidney, excretion of intact peptides in the urine did not appear to be a major route of clearance.
CC 13-7 (Mammalian Biochemistry)
ST lipoprotein **peptide** analog blood clearance; amphipathic **peptide** plasma clearance
IT Lipids, biological studies
RL: BIOL (Biological study)
(amphipathic **peptide** association with, in blood, rate of metabolism in relation to)
IT Urine

(amphipathic **peptide** elimination in, from blood, lipoprotein metabolism in relation to)

IT Lipophilicity
(amphipathic **peptide** metabolism in blood in relation to)

IT Kidney, metabolism
Liver, metabolism
(amphipathic **peptide** uptake by, from blood, lipoprotein metabolism in relation to)

IT **Peptides**, biological studies
RL: BIOL (Biological study)
(amphipathic, metabolism of, in blood, lipophilicity in relation to)

IT Lipoproteins
RL: BIOL (Biological study)
(apo-, **peptide** analogs of, metabolism of, in blood)

IT Lipoproteins
RL: BIOL (Biological study)
(high-d., amphipathic **peptide** association with, in blood, metabolism in relation to)

IT Conformation and Conformers
(α-helical, of amphipathic **peptides**, lipid effect on)

=>